WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Thursday, June 01, 2006

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ	
☐	L23	(L22 and (signal or leader sequence))	48
☐	L22	(L20 and (cleavable linker or peptide))	52
☐	L21	(L20 and (propeptide or proprotein))	0
☐	L20	(recombinant Fab fragment)	54
☐	L19	(L18 and (propeptide or proprotein))	55
☐	L18	(L17 and (cleavable linker or peptide))	196
☐	L17	(L16 and antibody)	196
☐	L16	(L15 and (Fd and LC))	196
☐	L15	(L14 and (leader sequence))	5849
☐	L14	(L13 and (signal peptide))	7945
☐	L13	((Fab fragment) and production)	19944
☐	L12	L11 and (Fab fragment)	5
☐	L11	L10 and propeptide	5
☐	L10	L9 and proprotein	54
☐	L9	L8 and (cleavable linker or peptide)	334
☐	L8	L7 and LC	334
☐	L7	L6 and Fd	3901
☐	L6	(L5 and signal)	11497
☐	L5	(L3 and leader)	11620
☐	L4	L3 and leader or signal	4581194
☐	L3	L2 and production	18616
☐	L2	L1 and recombinant	19323
☐	L1	Fab fragment	21705

END OF SEARCH HISTORY

WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Monday, June 05, 2006

Hide?	Set Name	Query	Hit Count
		DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ	
☐	L17	L14 and cleavable	0
☐	L16	L14 and prepro	0
☐	L15	L14 and proprotein	0
☐	L14	multimeric diabody	3
☐	L13	(L12 and (proprotein))	1
☐	L12	(l11 and (cleavable peptide))	41
☐	L11	(diabody and (cleavable peptide))	41
☐	L10	(L9 and (proprotein))	1
☐	L9	(L8 and (host cell))	20
☐	L8	(L5 and (leader sequence))	20
☐	L7	(L5 and (signal peptide) or (leader sequence))	24309
☐	L6	L5 or (cleavable linker)	4304
☐	L5	L3 and (cleavable peptide)	33
☐	L4	L3 and (cleavable peptide) or (cleavable linker)	4304
☐	L3	L2 and (peptide linker)	179
☐	L2	L1 and (cleav?)	2882
☐	L1	diabody	4489

END OF SEARCH HISTORY

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                     Welcome to DialogClassic Web(tm)
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Logon file001 01jun06 12:36:29
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***Index Chemicus (File 302)
***Inspec (File 202)

RESUMED UPDATING
***File 141, Reader's Guide Abstracts
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***File 523, D&B European Dun's Market Identifiers
***File 531, American Business Directory
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*** The 2005 reload of the CLAIMS files (Files 340, 341, 942)
is now available online.
                             ***
DATABASES REMOVED
***File 196, FINDEX
***File 468, Public Opinion Online (POLL)
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Data Report (F452), Prous Science Drugs of the Future (F453),
IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein
Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus
(File 302).
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File   1:ERIC 1966-2006/Apr (c) format only 2006 Dialog

      Set  Items  Description
      ---  -----  -----------
Cost is in DialUnits
?

B 155, 159, 10, 203, 35, 5, 467, 73, 434, 34
       01jun06 12:36:59 User290558 Session D48.1
            $0.81    0.232 DialUnits File1
     $0.81  Estimated cost File1
     $0.13  INTERNET
     $0.94  Estimated cost this search
     $0.94  Estimated total session cost   0.232 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R) 1951-2006/May 31
         (c) format only 2006 Dialog
 *File 155: Please see HELP NEWS 154
for information about recent updates added to MEDLINE.
  File 159:Cancerlit 1975-2002/Oct
         (c) format only 2002 Dialog
 *File 159: Cancerlit is no longer updating.
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Please see HELP NEWS159.
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  File   5:Biosis Previews(R) 1969-2006/May W4
         (c) 2006 The Thomson Corporation
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         (c) 2001 Informania Ltd.
 *File 467: F467 will close on February 1, 2006.                        7.
  File  73:EMBASE 1974-2006/Jun 01
         (c) 2006 Elsevier Science B.V.
  File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
         (c) 1998 Inst for Sci Info
  File  34:SciSearch(R) Cited Ref Sci 1990-2006/May W3
         (c) 2006 Inst for Sci Info

      Set  Items  Description
      ---  -----  -----------
?

S ((FAB (N) FRAGMENT) OR ANTIBODY) AND RECOMBINANT)
>>>Unmatched parentheses
?

S (((FAB (N) FRAGMENT) AND ANTIBODY) AND RECOMBINANT
>>>Unmatched parentheses
?

S (FAB (N) FRAGMENT) AND ANTIBODY
           63470  FAB
          522172  FRAGMENT
            7360  FAB(N)FRAGMENT
         1753124  ANTIBODY
      S1    5924  (FAB (N) FRAGMENT) AND ANTIBODY
?

S (FD AND FAB)
           18947  FD
           63470  FAB
      S2     677  (FD AND FAB)
?

S (PROPROTEIN OR PROPEPTIDE)
            4311  PROPROTEIN
           14326  PROPEPTIDE
      S3   18280  (PROPROTEIN OR PROPEPTIDE)
?


Set      Items   Description
S1        5924   (FAB (N) FRAGMENT) AND ANTIBODY
S2         677   (FD AND FAB)
S3       18280   (PROPROTEIN OR PROPEPTIDE)
?

S (SIGNAL (N) PEPTIDE) OR (LEADER (N) SEQUENCE)
         1320878  SIGNAL
         1140602  PEPTIDE
           37493  SIGNAL(N)PEPTIDE
           52265  LEADER
         2586500  SEQUENCE
           10118  LEADER(N)SEQUENCE
      S4   46929  (SIGNAL (N) PEPTIDE) OR (LEADER (N) SEQUENCE)
?


Set     Items   Description
S1       5924   (FAB (N) FRAGMENT) AND ANTIBODY
S2        677   (FD AND FAB)
S3      18280   (PROPROTEIN OR PROPEPTIDE)
S4      46929   (SIGNAL (N) PEPTIDE) OR (LEADER (N) SEQUENCE)
?

S S1 AND S2 AND S3 AND S4
            5924  S1
             677  S2
           18280  S3
           46929  S4
      S5       0  S1 AND S2 AND S3 AND S4
?


Set     Items   Description
S1       5924   (FAB (N) FRAGMENT) AND ANTIBODY
S2        677   (FD AND FAB)
S3      18280   (PROPROTEIN OR PROPEPTIDE)
S4      46929   (SIGNAL (N) PEPTIDE) OR (LEADER (N) SEQUENCE)
S5          0   S1 AND S2 AND S3 AND S4
?

S S2 AND S3 AND S4
             677  S2
           18280  S3
           46929  S4
      S6       0  S2 AND S3 AND S4
?


Set     Items   Description
S1       5924   (FAB (N) FRAGMENT) AND ANTIBODY
S2        677   (FD AND FAB)
S3      18280   (PROPROTEIN OR PROPEPTIDE)
S4      46929   (SIGNAL (N) PEPTIDE) OR (LEADER (N) SEQUENCE)
S5          0   S1 AND S2 AND S3 AND S4
S6          0   S2 AND S3 AND S4
?

S S2 AND S3
             677  S2
           18280  S3
      S7       0  S2 AND S3
?


Set     Items   Description
S1       5924   (FAB (N) FRAGMENT) AND ANTIBODY
S2        677   (FD AND FAB)
```

```
S3      18280   (PROPROTEIN OR PROPEPTIDE)
S4      46929   (SIGNAL (N) PEPTIDE) OR (LEADER (N) SEQUENCE)
S5          0   S1 AND S2 AND S3 AND S4
S6          0   S2 AND S3 AND S4
S7          0   S2 AND S3
?

S S2 AND S4
              677  S2
            46929  S4
      S8       26  S2 AND S4
?

RD S8
      S9        9  RD S8  (unique items)
?

TYPE S9/MEDIUM,K/1-9
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9/K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

12582750 PMID: 10607894
An approach for preventing recombination-deletion of the 40-50 anti-digoxin antibody V(H) gene from the phage display vector pComb3.
Kim S H; Titlow C C; Margolies M N
Department of Surgery, Massachusetts General Hospital and Harvard Medical School, Boston, MA 02114, USA.
Gene (NETHERLANDS) Jan 4 2000, 241 (1) p19-25, ISSN 0378-1119--Print Journal Code: 7706761
Contract/Grant No.: HL47415; HL; NHLBI
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

... Ig) genes. As an approach to circumvent the recombination-deletion of the murine anti-digoxin Fab 40-50 cloned into the pComb3 vector, the vector was modified with short synthetic oligonucleotides by replacing a pelB leader sequence with a gene 3 (g3) leader sequence and by using a single lacZ promoter sequence. By this means, the N-terminal amino acids of the L chain and Fd remained unchanged, and a random HCDR3 library built on this newly designed vector did not...

9/K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

11550165 PMID: 9390457
Efficient production of a functional mouse/human chimeric Fab' against human urokinase-type plasminogen activator by Bacillus brevis.
Inoue Y; Ohta T; Tada H; Iwasa S; Udaka S; Yamagata H
Department of Applied Biological Sciences, Faculty of Agriculture, Nagoya University, Japan.
Applied microbiology and biotechnology (GERMANY) Oct 1997, 48 (4) p487-92, ISSN 0175-7598--Print Journal Code: 8406612
Publishing Model Print

Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

Efficient production of a functional mouse/human chimeric Fab ' against human urokinase-type plasminogen activator by Bacillus brevis.

Expression/secretion vectors for the production of Fab ' and single-chain (sc) Fab ' by Bacillus brevis have been constructed. For the production of Fab ', the cDNAs encoding the L chain and Fd ' fragment (Fd with the hinge region) of a mouse-human chimeric Fab ' against human urokinase-type plasminogen activator were fused directly with the translation-start and signal - peptide -encoding regions of the mwp gene, the gene for one of the major cell-wall...

... peptide linker of 17 or 24 amino acids, and fused with the translation start and signal - peptide -encoding regions of the mwp gene. Fab ' was efficiently produced by B. brevis, being accumulated at a level of 100 mg/l ...

...remained at a level of a few milligrams per liter in the culture medium. The Fab ' produced by B. brevis showed comparable antigen-binding activity to that of the parental antibody. The L chain and Fd ' fragment, constituting the Fab ', had the correct N-terminal amino acid sequences. These results indicate that B. brevis is...

Descriptors: *Bacillus--metabolism--ME; *Immunoglobulin Fab Fragments --immunology--IM; *Immunoglobulin G--immunology--IM; *Recombinant Fusion Proteins--immunology--IM; *Urinary Plasminogen Activator...
; Amino Acid Sequence; Animals; Antibody Specificity; Base Sequence; Genes, Bacterial; Genes, Synthetic; Humans; Immunoglobulin Fab Fragments --biosynthesis--BI; Immunoglobulin Fab Fragments--genetics--GE; Immunoglobulin Fab Fragments--isolation and purification--IP; Immunoglobulin G--biosynthesis--BI; Immunoglobulin G--genetics--GE; Immunoglobulin G...

Chemical Name: Immunoglobulin Fab Fragments; Immunoglobulin G; Recombinant Fusion Proteins; Urinary Plasminogen Activator

9/K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

10606195 PMID: 8536316
Multiple roles of the cellulase CBHI in enhancing production of fusion antibodies by the filamentous fungus Trichoderma reesei.
Nyyssonen E; Keranen S
VTT Biotechnology and Food Research, Finland.
Current genetics (UNITED STATES) Jun 1995, 28 (1) p71-9, ISSN 0172-8083--Print Journal Code: 8004904
Publishing Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

The production of Fab antibody fragments in Trichoderma reesei can be increased over 50-fold by fusing the core-linker region of the T. reesei cellulase CBHI (cellobiohydrolase I) to the heavy Fd chain (Nyyssonen et al. 1993). This beneficial role of CBHI in antibody production has now been studied further by comparisons of T. reesei trains producing the light chain only. Fab or CBHI- Fab all of which exhibited identical light chain integration. The N-terminal fusion of CBHI to the heavy Fd chain not only aided secretion, as expected, but also increased the level of mRNA encoding the CBHI-heavy Fd chain, either by stabilizing the messenger or by enhancing transcription. The CBHI part appeared to...

... secretion at least by aiding the passage through the endoplasmic reticulum, since processing of the signal peptide of the antibody chains seemed to be most efficient in the strain producing CBHI- Fab in contrast to the strains producing light chain or Fab fragment. Interestingly, CBHI core-linker protein, originating from the CBHI-heavy Fd chain, was found in large amounts in the culture medium. The cleavage resulting in this...

Descriptors: *Glycoside Hydrolases--metabolism--ME; *Immunoglobulin Fab Fragments--genetics--GE; *Trichoderma--genetics--GE; Cellulose 1,4-beta-Cellobiosidase; Cloning, Molecular; Culture Media; Genetic Vectors; Immunoglobulin Fab Fragments--biosynthesis--BI; RNA, Messenger--genetics --GE; RNA, Messenger--metabolism--ME; Recombinant Fusion Proteins --genetics...

Chemical Name: Culture Media; Genetic Vectors; Immunoglobulin Fab Fragments; RNA, Messenger; Recombinant Fusion Proteins; Glycoside Hydrolases; Cellulose 1,4-beta-Cellobiosidase

9/K/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

(c) format only 2006 Dialog. All rts. reserv.

09604489 PMID: 7763534

High-level production and secretion of a mouse-human chimeric Fab fragment with specificity to human carcino embryonic antigen in Escherichia coli.

Shibui T; Munakata K; Matsumoto R; Ohta K; Matsushima R; Morimoto Y; Nagahari K

Biosciences Laboratory, Mitsubishi Kasei Corporation, Kanagawa, Japan.

Applied microbiology and biotechnology (GERMANY) Mar 1993, 38 (6) p770-5, ISSN 0175-7598--Print Journal Code: 8406612

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

High-level production and secretion of a mouse-human chimeric Fab fragment with specificity to human carcino embryonic antigen in Escherichia coli.

...high-level secretion system for the production of mouse-human chimeric antibody 21B2 (MHC 21B2) Fab fragment specific for human carcino embryonic antigen (hCEA) in Escherichia coli has been constructed. The genes encoding a light chain and an Fd fragment (a variable region and the CH1 domain of a heavy chain) of a mouse-human chimeric antibody were directly fused to the signal peptide of the E. coli ompF gene sequence. E. coli cells containing expression vectors in which...

... located downstream of a separate tac promoter were able to secrete the light chain and Fd fragment as two of their major cellular proteins. The signal peptides were efficiently removed from...

... high-cell-density culture experiments using a jar fermentor, the amount of light chain and Fd fragment produced was at levels of up to 2.88 g/l and 1.28...

... encourage correct folding, formation of disulphide bonds, and association of the light chain with the Fd fragment, we have established a procedure that can purify, re-fold, and combine aggregated products to electrophoretically homogeneous Fab fragment with a yield of approximately 47%. Fab fragment produced in this manner shows essentially the same antigen-binding activity and specificity to...

Descriptors: *Carcinoembryonic Antigen--immunology--IM; *Escherichia coli --genetics--GE; *Immunoglobulin Fab Fragments--biosynthesis--BI; Amino Acid Sequence; Animals; Antibody Affinity; Antibody Specificity; Biotechnology; Genes, Immunoglobulin; Genetic Vectors; Humans; Immunoglobulin Fab Fragments--genetics--GE; Immunoglobulin Fab Fragments--isolation and purification--IP; Mice; Molecular Sequence Data; Recombinant Proteins--biosynthesis--BI; Recombinant Proteins...

Chemical Name: Carcinoembryonic Antigen; Genetic Vectors; Immunoglobulin Fab Fragments; Recombinant Proteins

9/K/5 (Item 5 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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09398379 PMID: 1368908

Secretion of a functional Fab fragment in Escherichia coli and the influence of culture conditions.

Shibui T; Nagahari K

Biosciences Laboratory, Mitsubishi Kasei Corporation, Kanagawa, Japan.

Applied microbiology and biotechnology (GERMANY) Jun 1992, 37 (3) p352-7, ISSN 0175-7598--Print Journal Code: 8406612

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Secretion of a functional Fab fragment in Escherichia coli and the influence of culture conditions.

Genes encoding a light chain and an Fd region (a variable region and a CH1 domain of a heavy chain) of a mouse...

...specificity for human carcinoembryonic antigen (CEA) were fused to a DNA segment coding for the signal peptide of Escherichia coli ompF. E. coli cells harbouring an expression vector containing these genes downstream of a tac promoter were able to secrete a Fab fragment of the antibody efficiently. When the cells were cultured at 37 degrees C and...

...inducer (isopropyl-beta-D-thiogalactopyranoside, IPTG) concentration was 1 mM (standard conditions), production of functional Fab was very low (medium; 200 ng/1 culture and periplasm; less than 90 ng/1 culture). In order to optimize functional Fab production, we examined the influence of culture conditions (i.e. temperature and the inducer concentration...

...secretion of the product. It was found that a 12.7-fold higher amount of Fab fragment could be produced at 30 degrees C using 0.1 mM IPTG, as compared with standard conditions. Under these optimal conditions, functional Fab accumulated in the periplasm and culture medium for 10 h after induction and the total...

Descriptors: *Escherichia coli--genetics--GE; *Genes, Immunoglobulin; *Immunoglobulin Fab Fragments--genetics--GE

Chemical Name: Carcinoembryonic Antigen; Culture Media; Immunoglobulin Fab Fragments; Plasmids; Recombinant Proteins; DNA

9/K/6 (Item 1 from file: 203)

DIALOG(R)File 203:AGRIS

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02090392 AGRIS No: 97-018278

Multiple roles of the cellulase CBH1 in enhancing production of fusion antibodies by the filamentous fungus Trichoderma reesei

Nyyssoenen, E.; Keraenen, S. (VTT Biotechnology and Food Research (Finland))

Journal: Current Genetics, 1995, v. 28(1) p. 71-79

Language: English Summary Language: English

The production of Fab antibody fragments in Trichoderma reesei can be increased over 50-fold by fusing the core-linker region of the T. reesei cellulase CBH1 (cellobiohydrolase 1) to the heavy Fd chain. This beneficial role of CBH1 in antibody production has now been studied further by comparisons of T. reesei strains producing the light chain only, Fab or CBH1- Fab all of which exhibited identical light chain integration. The N-terminal fusion of CBH1 to the heavy Fd chain not only aided secretion, as expected, but also increased the level of mRNA encoding the CBH1-heavy Fd chain, either by stabilizing the messenger or by enhancing transcription. The CBH1 part appeared to...

... secretion at least by aiding the passage through the endoplasmic reticulum, since processing of the signal peptide of the antibody chains seemed to be most efficient in the strain producing CBH1- Fab in contrast to the strains producing light chain or Fab fragment. Interestingly, CBH1 core-linker protein, originating from the CBH1-heavy Fd chain, was found in large amounts in the culture medium. The cleavage resulting in this...

9/K/7 (Item 1 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

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0012413796 BIOSIS NO.: 200000132109

An approach for preventing recombination-deletion of the 40-50 anti-digoxin antibody VH gene from the phage display vector pComb3

AUTHOR: Kim Se-Ho; Titlow Christian C; Margolies Michael N (Reprint)

AUTHOR ADDRESS: Antibody Engineering Laboratory, MGH East, 149 13th Street, Charlestown, MA, 02129, USA**USA

JOURNAL: Gene (Amsterdam) 241 (1): p19-25 Jan. 4, 2000 2000

MEDIUM: print

ISSN: 0378-1119

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

...ABSTRACT: Ig) genes. As an approach to circumvent the recombination-deletion of the murine anti-digoxin Fab 40-50 cloned into the pComb3 vector, the vector was modified with short synthetic oligonucleotides by replacing a pelB leader sequence with a gene 3 (g3) leader sequence and by using a single lacZ promoter sequence. By this means, the N-terminal amino acids of the L chain and Fd remained unchanged, and a random HCDR3 library built on this newly designed vector did not...

9/K/8 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2006 Elsevier Science B.V. All rts. reserv.

06154151 EMBASE No: 1995193805
Extracellular expression of native human anti-lysozyme fragments in Staphylococcus carnosus
Schnappinger D.; Geissdorfer W.; Sizemore C.; Hillen W.
Lehrstuhl fur Mikrobiologie, Institut fur Mikrobiologie, BGFAUEN, Staudtstr. 5,91058 Erlangen Germany
FEMS Microbiology Letters (FEMS MICROBIOL. LETT.) (Netherlands) 1995, 129/2-3 (121-128)
CODEN: FMLED ISSN: 0378-1097
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

...to permit removal of the pro sequence. Extracellular expression of the light chain and the Fd fragment of a chimeric Fab fragment containing the variable regions of the anti-lysozyme antibody D1.3 was achieved with ...

...removed from the expression product by IgA protease treatment. When the light chain and the Fd fragment were co-secreted as a protein fusion they accumulated in a structure capable of...
...the pre-pro sequence followed by the light chain, a second IgA site and the Fd fragment.
DRUG DESCRIPTORS:
*immunoglobulin f(ab) fragment; *lysozyme; * signal peptide ; *xylose

9/K/9 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2006 Elsevier Science B.V. All rts. reserv.

05177020 EMBASE No: 1992317254
A recombinant human Fab expressed in Escherichia coli neutralizes rabies virus
Cheung S.C.; Dietzschold B.; Koprowski H.; Notkins A.L.; Rando R.F.
Triplex Pharmaceutical Corp., 9391 Grogan's Mill Rd.,Woodlands, TX 77380 United States
Journal of Virology (J. VIROL.) (United States) 1992, 66/11 (6714-6720)
CODEN: JOVIA ISSN: 0022-538X
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

A recombinant human Fab expressed in Escherichia coli neutralizes rabies virus

A recombinant human anti-rabies monoclonal antibody (MAb-57) Fab was prepared by cloning the heavy (Fd)- and light-chain domains into the same bacterial expression vector. To construct the recombinant Fab , mRNA was extracted from MAb-57-producing hybridoma cells, reverse transcribed, and then amplified by...
...PCR) by using oligonucleotides specific for immunoglobulin heavy- and light-chain DNA sequences. PCR- amplified Fd -chain cDNA was fused, in frame, between a bacterial leader peptide (PelB) at the amino...

```
...PCR-amplified lambda-chain cDNA was also fused to the PelB leader
peptide. The immunoglobulin  Fab  was then expressed as a dicistronic
message in bacteria by using the isopropyl-beta-D...

...V(H) (V(H)I) chain and V(L) (VlambdaII) chain gene usage. The
recombinant  Fab  (rFab57) specifically bound the rabies virus coat
glycoprotein, while the  Fd  and lambda chains, when expressed
individually, did not. The binding specificity of rFab57 was
indistinguishable...

...rFab was capable of neutralizing rabies virus strain CVS-11. We conclude
that a human  Fab  expressed in bacteria maintains its specificity and
biologic activity.
DRUG DESCRIPTORS:
...chain--endogenous compound--ec; immunoglobulin light chain--endogenous
compound--ec; protein g--endogenous compound--ec;  signal   peptide
--endogenous compound--ec
?

TYPE S9/FULL/2 AND 4
>>>'AND' not allowed in command
?

TYPE S9/FULL/2, 4

  9/9/2     (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2006 Dialog. All rts. reserv.

11550165   PMID: 9390457
 Efficient  production  of  a functional mouse/human chimeric Fab' against
 human urokinase-type plasminogen activator by Bacillus brevis.
  Inoue Y; Ohta T; Tada H; Iwasa S; Udaka S; Yamagata H
  Department of Applied Biological Sciences, Faculty of Agriculture, Nagoya
University, Japan.
  Applied  microbiology  and  biotechnology (GERMANY)   Oct  1997,  48  (4)
 p487-92,  ISSN 0175-7598--Print   Journal Code: 8406612
  Publishing Model Print
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed
  Subfile:   BIOTECHNOLOGY
  Expression/secretion  vectors for the production of Fab' and single-chain
(sc)  Fab'  by Bacillus brevis have been constructed. For the production of
Fab',  the  cDNAs  encoding the L chain and Fd' fragment (Fd with the hinge
region)  of  a  mouse-human  chimeric  Fab'  against  human  urokinase-type
plasminogen  activator  were  fused directly with the translation-start and
signal-peptide-encoding  regions  of  the mwp gene, the gene for one of the
major  cell-wall  proteins  of  Bacillus  brevis.  The two fused genes were
placed  tandemly downstream from the promoter of the cell-wall protein gene
operon (cwp) of B. brevis. For the production of scFab', the two cDNAs were
linked  with a synthetic oligonucleotide encoding a flexible peptide linker
of  17  or  24  amino  acids,  and  fused  with  the  translation start and
signal-peptide-encoding  regions  of  the  mwp  gene.  Fab' was efficiently
produced  by  B.  brevis,  being  accumulated at a level of 100 mg/l in the
culture  medium in a simple shake-flask culture, which is the highest level
obtained  so  far  for  a  gram-positive  bacterium. On the other hand, the
scFab'  remained  at  a  level of a few milligrams per liter in the culture
```

medium. The Fab' produced by B. brevis showed comparable antigen-binding activity to that of the parental antibody. The L chain and Fd' fragment, constituting the Fab', had the correct N-terminal amino acid sequences. These results indicate that B. brevis is a very promising host for the production of native Ig fragments.

Descriptors: *Bacillus--metabolism--ME; *Immunoglobulin Fab Fragments --immunology--IM; *Immunoglobulin G--immunology--IM; *Recombinant Fusion Proteins--immunology--IM; *Urinary Plasminogen Activator--immunology--IM; Amino Acid Sequence; Animals; Antibody Specificity; Base Sequence; Genes, Bacterial; Genes, Synthetic; Humans; Immunoglobulin Fab Fragments --biosynthesis--BI; Immunoglobulin Fab Fragments--genetics--GE; Immunoglobulin Fab Fragments--isolation and purification--IP; Immunoglobulin G--biosynthesis--BI; Immunoglobulin G--genetics--GE; Immunoglobulin G--isolation and purification--IP; Mice; Molecular Sequence Data; Promoter Regions (Genetics); Recombinant Fusion Proteins --biosynthesis--BI; Recombinant Fusion Proteins --isolation and purification--IP; Research Support, Non-U.S. Gov't

CAS Registry No.: 0 (Immunoglobulin Fab Fragments); 0 (Immunoglobulin G); 0 (Recombinant Fusion Proteins)

Enzyme No.: EC 3.4.21.73 (Urinary Plasminogen Activator)

Record Date Created: 19980127

Record Date Completed: 19980127

9/9/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

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09604489 PMID: 7763534

High-level production and secretion of a mouse-human chimeric Fab fragment with specificity to human carcino embryonic antigen in Escherichia coli.

Shibui T; Munakata K; Matsumoto R; Ohta K; Matsushima R; Morimoto Y; Nagahari K

Biosciences Laboratory, Mitsubishi Kasei Corporation, Kanagawa, Japan.

Applied microbiology and biotechnology (GERMANY) Mar 1993, 38 (6) p770-5, ISSN 0175-7598--Print Journal Code: 8406612

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: BIOTECHNOLOGY

A high-level secretion system for the production of mouse-human chimeric antibody 21B2 (MHC 21B2) Fab fragment specific for human carcino embryonic antigen (hCEA) in Escherichia coli has been constructed. The genes encoding a light chain and an Fd fragment (a variable region and the CH1 domain of a heavy chain) of a mouse-human chimeric antibody were directly fused to the signal peptide of the E. coli ompF gene sequence. E. coli cells containing expression vectors in which each of the two genes are located downstream of a separate tac promoter were able to secrete the light chain and Fd fragment as two of their major cellular proteins. The signal peptides were efficiently removed from the primary products by post-translational processing, although they formed insoluble aggregates, possibly in the periplasm. In high-cell-density culture experiments using a jar fermentor, the amount of light chain and Fd fragment produced was at levels of up to 2.88 g/l and 1.28 g/l culture, respectively. By optimizing the conditions that encourage correct folding, formation of disulphide bonds, and association of the light chain with the Fd fragment, we have established a procedure that can purify, re-fold, and combine aggregated products to electrophoretically homogeneous Fab fragment with a yield of approximately 47%. Fab fragment produced in this manner shows essentially the same antigen-binding activity and specificity to hCEA as the parental mouse antibody 21B2 (MoAb 21B2).

Descriptors: *Carcinoembryonic Antigen--immunology--IM; *Escherichia coli --genetics--GE; *Immunoglobulin Fab Fragments--biosynthesis--BI; Amino Acid Sequence; Animals; Antibody Affinity; Antibody Specificity; Biotechnology; Genes, Immunoglobulin; Genetic Vectors; Humans; Immunoglobulin Fab Fragments--genetics--GE; Immunoglobulin Fab Fragments --isolation and purification--IP; Mice; Molecular Sequence Data; Recombinant Proteins --biosynthesis--BI; Recombinant Proteins--genetics--GE; Recombinant Proteins--isolation and purification--IP

CAS Registry No.: 0 (Carcinoembryonic Antigen); 0 (Genetic Vectors); 0 (Immunoglobulin Fab Fragments); 0 (Recombinant Proteins)

Gene Symbol: ompF; tac

Record Date Created: 19930511

Record Date Completed: 19930511

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?


Set     Items   Description
S1       5924   (FAB (N) FRAGMENT) AND ANTIBODY
S2        677   (FD AND FAB)
S3      18280   (PROPROTEIN OR PROPEPTIDE)
S4      46929   (SIGNAL (N) PEPTIDE) OR (LEADER (N) SEQUENCE)
S5          0   S1 AND S2 AND S3 AND S4
S6          0   S2 AND S3 AND S4
S7          0   S2 AND S3
S8         26   S2 AND S4
S9          9   RD S8  (unique items)
?
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 NEWS  8  MAR 03  Updates in PATDPA; addition of IPC 8 data without attributes
 NEWS  9  MAR 22  EMBASE is now updated on a daily basis
 NEWS 10  APR 03  New IPC 8 fields and IPC thesaurus added to PATDPAFULL
 NEWS 11  APR 03  Bibliographic data updates resume; new IPC 8 fields and IPC
                  thesaurus added in PCTFULL
 NEWS 12  APR 04  STN AnaVist $500 visualization usage credit offered
 NEWS 13  APR 12  LINSPEC, learning database for INSPEC, reloaded and enhanced
 NEWS 14  APR 12  Improved structure highlighting in FQHIT and QHIT display
                  in MARPAT
 NEWS 15  APR 12  Derwent World Patents Index to be reloaded and enhanced during
                  second quarter; strategies may be affected
 NEWS 16  MAY 10  CA/CAplus enhanced with 1900-1906 U.S. patent records
 NEWS 17  MAY 11  KOREAPAT updates resume
 NEWS 18  MAY 19  Derwent World Patents Index to be reloaded and enhanced
 NEWS 19  MAY 30  IPC 8 Rolled-up Core codes added to CA/CAplus and
                  USPATFULL/USPAT2
 NEWS 20  MAY 30  The F-Term thesaurus is now available in CA/CAplus

 NEWS EXPRESS     FEBRUARY 15 CURRENT VERSION FOR WINDOWS IS V8.01a,
                  CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
                  AND CURRENT DISCOVER FILE IS DATED 19 DECEMBER 2005.
                  V8.0 AND V8.01 USERS CAN OBTAIN THE UPGRADE TO V8.01a AT
                  http://download.cas.org/express/v8.0-Discover/

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FILE 'HOME' ENTERED AT 13:19:27 ON 01 JUN 2006

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=> s (recombinant antibody) or (recombinant Fab fragment)
L1          4397 (RECOMBINANT ANTIBODY) OR (RECOMBINANT FAB FRAGMENT)

=> s (cleavable (linker or peptide))
MISSING OPERATOR 'CLEAVABLE (LINKER'
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s (cleavable (w) (linker or peptide))
L2           618 (CLEAVABLE (W) (LINKER OR PEPTIDE))

=> s ((signal or leader) (w) sequence)
L3         29266 ((SIGNAL OR LEADER) (W) SEQUENCE)

=> d his

     (FILE 'HOME' ENTERED AT 13:19:27 ON 01 JUN 2006)

     FILE 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE' ENTERED AT
     13:20:11 ON 01 JUN 2006
L1           4397 S (RECOMBINANT ANTIBODY) OR (RECOMBINANT FAB FRAGMENT)
L2            618 S (CLEAVABLE (W) (LINKER OR PEPTIDE))
L3          29266 S ((SIGNAL OR LEADER) (W) SEQUENCE)

=> s L1 and L2 and L3
L4             0 L1 AND L2 AND L3

=> s propeptide or proprotein
L5          9391 PROPEPTIDE OR PROPROTEIN

=> s l1 and l3 and l5
L6             0 L1 AND L3 AND L5

=> s l2 and l5
L7             2 L2 AND L5

=> s l3 and l5
L8           411 L3 AND L5

=> s (antibody or (Fab (w) fragment)) and l8
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L9          44 (ANTIBODY OR (FAB (W) FRAGMENT)) AND L8

=> duplicate remove l9
DUPLICATE PREFERENCE IS 'CAPLUS, BIOTECHNO, BIOTECHDS, ESBIOBASE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L9
L10          27 DUPLICATE REMOVE L9 (17 DUPLICATES REMOVED)

=> d l10 bib abs 1-27

L10  ANSWER 1 OF 27  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2006:318526  CAPLUS
DN   144:344946
TI   Molecular toxicity models based on gene expression profiles in isolated
     rat hepatocytes exposed to known hepatotoxins
IN   Higgs, Brandon; Elashoff, Michael; Mendrick, Donna L.; Porter, Mark W.;
     Castle, Arthur L.; Johnson, Kory R.
PA   Gene Logic, Inc., USA
SO   PCT Int. Appl., 271 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   WO 2006037025        A2    20060406    WO 2005-US34780        20050928
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
             LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ,
             NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
             SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,
             YU, ZA, ZM, ZW
         RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
             IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
             CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
             GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM
PRAI US 2004-613292P      P     20040928
AB   The present invention includes methods of predicting hepatotoxicity of
     test agents and methods of generating hepatotoxicity prediction models
     using algorithms for analyzing quant. gene expression information.
     Isolated Sprague-Dawley rat hepatocytes exposed to known hepatotoxins were
     examined to identify changes in genes expression induced by these compds.
     using the Affymetrix Rat Microarray.  These changes in gene expression
     provide useful toxicity markers than can be used to monitor toxicity
     and/or toxicity progression by a test compound  Some of these markers may
     also be used to monitor or detect various disease or physiol. states,
     disease progression, drug efficacy, and drug metabolism  The invention also
     includes microarrays, computer systems comprising the toxicity prediction
     models, as well as methods of using the computer systems by remote users
     for determining the toxicity of test agents.

L10   ANSWER 2 OF 27  BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN    2005-14577  BIOTECHDS
TI    New muscle-targeting fusion protein for treating muscle-related diseases,
      e.g. muscle atrophy, comprises a ligand that binds a target surface
      protein; a therapeutic agent; and a multimerizing component and/or a
      signal sequence;
         muscle-targeting fusion protein gene transfer and expression in host
         cell for muscle-related condition or disease gene therapy
AU    GLASS D J
PA    REGENERON PHARM INC
PI    WO 2005033134 14 Apr 2005
```

AI WO 2004-US32233 30 Sep 2004
PRAI US 2004-584956 2 Jul 2004; US 2003-507168 30 Sep 2003
DT Patent
LA English
OS WPI: 2005-285404 [29]
AN 2005-14577 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - A targeting fusion polypeptide comprising a first component comprising a targeting ligand, or its derivative or fragment, capable of binding specifically to a pre-selected cell surface protein; a second component comprising at least one active or therapeutic agent; and optionally, a multimerizing component capable of forming a multimer with another targeting fusion polypeptide; and/or a **signal sequence**, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) an isolated nucleic acid molecule encoding the above fusion polypeptide; and (2) a pharmaceutical composition comprising the above fusion polypeptide and a carrier.

WIDER DISCLOSURE - Also disclosed are: (a) a vector comprising the above nucleic acid molecule; (b) a method of producing the above fusion polypeptide; (c) a method of treating a disease or condition; and (d) a method for activating and/or phosphorylating multiple cell receptors simultaneously.

BIOTECHNOLOGY - Preferred Fusion Polypeptide: The fusion polypeptide is a muscle-targeting fusion polypeptide, and the cell surface protein is a muscle cell surface protein. The targeting fusion polypeptide further comprises a second active or therapeutic agent. The targeting ligand comprises 3 N-terminal cadherin domains of human M-cadherin. The muscle surface protein is a receptor. The receptor is MuSK and the targeting ligand is agrin or a fragment of agrin capable of binding the MuSK receptor, or an anti-MuSK **antibody** or its mutant, fragment or derivative having biological activity. The fusion polypeptide may be a combined therapeutic fusion polypeptide, which comprises a first active or therapeutic agent, and a second active or therapeutic agent; and optionally, a multimerizing component capable of forming a multimer with another therapeutic fusion polypeptide, and/or a **signal sequence**. The first or second active or therapeutic agent is an activating **antibody** or a blocking **antibody**. The blocking **antibody** blocks a component selected from myostatin, activin receptor, BMP receptor 1, TNF receptor and IL-1 receptor. The activating **antibody** activates a component selected from IGF1 receptor, B2-adrenergic receptor and the IL-15 receptor complex. The first and/or second active or therapeutic agent is a ligand for a cell surface receptor, and is capable of binding and activating the cell surface receptor. The active or therapeutic agent is selected from IL-15, myotrophin, urocortin, urocortin II, a natural or mutant human IGF1 or IGF2, insulin, human myostatin **propeptide**, hGH, proliferin, follistatin, FSTL1, and FLRG, or its mutant, derivative or fragment having biologically activity. The mutant human IGF1 comprises a modification selected from delGPE (1-3), E3R and E3A; and a modification selected from R36A, R37A, del36 and del37. The first active or therapeutic agent is hGH and the second active or therapeutic agent is the mutant human IGF1 as mentioned above. The fusion polypeptide may be IGF1-related fusion polypeptide comprising the human IGF1 comprising the modification mentioned above; a multimerizing component capable of forming a multimer with another IGF-related polypeptide; and optionally, a **signal sequence**. Alternatively, the fusion polypeptide is a myostatin inhibiting fusion polypeptide comprising (P)x-M, P = human myostatin **propeptide**, or its fragment or variant, capable of binding and inhibiting the biological activity of myostatin; M = multimerizing component; and X = 1-10. The multimerizing component of the targeting fusion polypeptide is selected from a multimerizing component comprising a cleavable region (C-region); a truncated multimerizing component; an amino acid sequence of 1-500 amino acids in length, optionally comprising at least one cysteine residue; a leucine zipper; a helix loop motif; a coil-coil motif; and an Fc-protein. The first component targeting ligand comprises 3 cadherin domains of a human cadherin. The human cadherin is selected from muscle cadherin (M-cadherin), nerve cadherin (N-cadherin), vascular endothelial cadherin (VE-cadherin), cadherin 17 (liver-intestine cadherin), cadherin 13 (heart cadherin), cadherin 26, cadherin 24 and epithelial cadherin (E-cadherin or cadherin-1). The first component may comprise 3 cadherin domains of human VE-cadherin. The second component active or therapeutic agent is vascular endothelial growth factor (VEGF), angiopoietin-1, angiopoietin-2, or their mutants, derivatives or fragments, having biological activity. The multimeric fusion polypeptide comprises 2 or more of the fusion polypeptides mentioned above.

ACTIVITY - Muscular-Gen. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The fusion protein is useful in therapy or in the manufacture of a medicament for the treatment of a muscle-related condition or disease in a subject suffering from a condition which would benefit from the medicament, such as muscle atrophy or muscle dystrophy (claimed).

ADMINISTRATION - Dosages may range from about 0.01 pg/kg-1 mg/kg of body weight. Administration can be intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, pulmonary, intranasal, intraocular, epidural, topical or oral.

EXAMPLE - No relevant example given. (84 pages)

L10 ANSWER 3 OF 27 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2005-14659 BIOTECHDS
TI New DNA construct comprising a sequence encoding an immunoglobulin signal peptide (SP)-tissue-type plasminogen activator (tPA) pre-**propeptide**, comprising an immunoglobulin SP fused to a tPA **propeptide**, useful for producing polypeptides;
involving vector-mediated gene transfer and expression in Chinese hamster ovary, baby hamster kidney, HEK-293 or NIH3T3 cell
AU DUPRAZ P; KOBR M
PA ARS APPLIED RES SYSTEMS HOLDING NV
PI WO 2005030963 7 Apr 2005
AI WO 2004-EP52302 24 Sep 2004
PRAI US 2003-506939 29 Sep 2003; EP 2003-103580 26 Sep 2003
DT Patent
LA English
OS WPI: 2005-273383 [28]
AN 2005-14659 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - A DNA construct comprising a sequence encoding an immunoglobulin signal peptide (IgSP)-tissue-type plasminogen activator (tPA) pre-**propeptide** comprising an IgSP fused to a tPA **propeptide**, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) a DNA construct comprising a sequence encoding a human tPA where the carboxyl-terminal extremity of the tPA **propeptide** consists of amino acids Arg-Xaa-Arg-Arg; (2) a host cell transformed with the DNA construct; (3) producing a polypeptide of interest comprising transfecting a host cell with the DNA construct, or culturing the host cell; and (4) a fusion polypeptide encoded by the DNA constructs.

BIOTECHNOLOGY - Preparation: No general preparation for the DNA construct is given. Preparation (claimed): Producing a polypeptide further comprises isolating the polypeptide of interest from the host cells. The transfection is stable transfection. Preferred Construct: The DNA construct comprises the immunoglobulin signal peptide, which is a murine immunoglobulin signal peptide. The murine immunoglobulin signal peptide comprises a sequence of 19 amino acids (SEQ ID Number 3), fully defined in the specification. The tPA **propeptide** is a human tPA **propeptide**, the carboxyl-terminal extremity of the tPA **propeptide** consisting of amino acids Arg-Xaa-Arg-Arg. The tPA

propeptide consists of amino acids 23 to 32 of a sequence of 35 amino acids (SEQ ID Number 2), fully defined in the specification. The pre-**propeptide** comprises a sequence of 29 amino acids (SEQ ID Number 1), fully defined in the specification. The DNA construct encodes a fusion polypeptide comprising the IgSP-tPA pre-**propeptide** fused to a polypeptide of interest. The DNA construct further comprises a **signal sequence** fused to the tPA **propeptide**.
The DNA construct encodes a fusion polypeptide comprising the tPA **propeptide** fused to a polypeptide of interest. The DNA construct is included in a vector. The vector is an expression vector. The vector is a vector for performing gene activation. Preferred Cell: The host cell is selected from CHO (Chinese hamster ovary) cell, a COS cell, a CV1 cell, a mouse L cell, a HT1080 cell, a BHK cell, a HEK293 cell, a N1H-3T3 cell, a LM cell and a Y1 cell, NSO and SP2/0 mouse hybridoma and the like, Namalwa, RPMI-8226, Vero, WI-38, and MRC-5. The host cell is preferably a CHO cell.

USE - The DNA construct is useful for producing polypeptide of interest (claimed).

ADVANTAGE - The DNA constructs are at least 2 fold more efficient in promoting secretion of proteins of interest than prior art **leader sequences**.(44 pages)

```
L10  ANSWER 4 OF 27  CAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 1
AN   2005:248644  CAPLUS
DN   142:274057
TI   Sequences of human schizophrenia related genes and use for diagnosis,
     prognosis and therapy
IN   Liew, Choong-chin
PA   Chondrogene Limited, Can.
SO   U.S. Pat. Appl. Publ., 156 pp., Cont.-in-part of U.S. Ser. No. 802,875.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 47
     PATENT NO.          KIND  DATE        APPLICATION NO.        DATE
     ---------------     ----  --------    --------------------   --------
PI   US 2004241727        A1   20041202    US 2004-812731         20040330
     US 2004014059        A1   20040122    US 2002-268730         20021009
     US 2005191637        A1   20050901    US 2004-803737         20040318
     US 2005196762        A1   20050908    US 2004-803759         20040318
     US 2005196763        A1   20050908    US 2004-803857         20040318
     US 2005196764        A1   20050908    US 2004-803858         20040318
     US 2005208505        A1   20050922    US 2004-803648         20040318
     US 2004241727        A1   20041202    US 2004-812731         20040330
PRAI US 1999-115125P      P    19990106
     US 2000-477148       B1   20000104
     US 2002-268730       A2   20021009
     US 2003-601518       A2   20030620
     US 2004-802875       A2   20040312
     US 2004-812731       A    20040330
AB   The present invention is directed to detection and measurement of gene
     transcripts and their equivalent nucleic acid products in blood.  Specifically
     provided is anal. performed on a drop of blood for detecting, diagnosing
     and monitoring diseases using gene-specific and/or tissue-specific
     primers.  The present invention also describes methods by which
     delineation of the sequence and/or quantitation of the expression levels
     of disease-specific genes allows for an immediate and accurate
     diagnostic/prognostic test for disease or to assess the effect of a
     particular treatment regimen.  [This abstract record is one of 3 records for
     this document necessitated by the large number of index entries required to
     fully index the document and publication system constraints.].

L10  ANSWER 5 OF 27  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2004:650066  CAPLUS
```

```
DN    141:185966
TI    Production of multimeric proteins using transposon-based vectors
      comprising protein monomer-encoding sequences linked by pro, prepro,
      and/or cleavage sequences
IN    Cooper, Richard K.; Fioretti, William C.; Cadd, Gary G.
PA    Transgenrx, Inc., USA; The Board of Supervisors of Louisiana State
      University and Agricultural and Mechanical College
SO    PCT Int. Appl., 119 pp.
      CODEN: PIXXD2
DT    Patent
LA    English
FAN.CNT 6
      PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
      ---------------     ----   --------    --------------------    --------
PI    WO 2004067706        A2    20040812    WO 2003-US41261         20031224
      WO 2004067706        A3    20041223
          W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
              CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
              GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
              LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
              NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
              TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
          RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
              BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
              ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
              TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
      US 2004197910        A1    20041007    US 2003-609019          20030626
      AU 2003303830        A1    20040823    AU 2003-303830          20031224
      EP 1597378           A2    20051123    EP 2003-808563          20031224
          R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
      JP 2006512921        T2    20060420    JP 2004-567446          20031224
PRAI  US 2003-441377P      P     20030121
      US 2003-441381P      P     20030121
      US 2003-441392P      P     20030121
      US 2003-441405P      P     20030121
      US 2003-441447P      P     20030121
      US 2003-441502P      P     20030121
      US 2003-609019       A     20030626
      US 2002-392415P      P     20020626
      WO 2003-US41261      W     20031224
AB    The present invention provides a new, effective, and efficient method of
      producing multimeric proteins in an individual.  Multimeric proteins
      include associated multimeric proteins (two or more associated polypeptides)
and
      multivalent multimeric proteins (a single polypeptide encoded by more than
      one gene of interest).  Expression and/or formation of the multimeric
      protein in the individual is achieved by administering a polynucleotide
      cassette containing genes of interest that encode portions of the multimeric
      protein to the individual.  The polynucleotide cassette may addnl. contain
      one or more pro sequences, prepro sequences, cecropin prepro sequences,
      and/or cleavage site sequences.  Two preferred transposon-based vectors,
      termed pTnMCS and pTnMod, produce integration frequencies an order of
      magnitude greather than has been achieved with previous vectors.  Quail
      and chickens containing a representative transposon-based vector containing a
CMV
      promoter/cecropin prepro/antibody heavy chain/ cecropin pro/
      antibody light chain/conalbumin poly(A) injected into the oviduct
      produced antibody in the egg white.

L10   ANSWER 6 OF 27  CAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 2
AN    2003:836512  CAPLUS
DN    139:333995
TI    Cloning of Aspergillus oryzae gap repair genes rdhA, rdhB and rdhD and
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     method of using them to improve recombination-mediated mutagenesis in
     filamentous fungal host
IN   Brody, Howard; Otani, Suzanne M.; Cherry, Joel R.
PA   Novozymes Biotech, Inc., USA
SO   U.S. Pat. Appl. Publ., 62 pp.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   US 2003199038        A1    20031023    US 2003-422013         20030422
     WO 2003089648        A1    20031030    WO 2003-US13577        20030422
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
             TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2003231228        A1    20031103    AU 2003-231228         20030422
     EP 1499733           A1    20050126    EP 2003-724363         20030422
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRAI US 2002-374688P      P     20020422
     WO 2003-US13577      W     20030422
AB   The present invention relates to methods for preparing variants of a
     nucleotide sequence, comprising: (a) introducing plasmids into a
     population of filamentous fungal host cells, and (b) cultivating the
     population of recombinant filamentous fungal cells in a medium suitable
     for growth; and (c) screening the population of recombinant filamentous
     fungal cells for variants of the DNA sequence contained on one or more
     autonomously replicating circularized plasmids.  The introduced plasmids
     comprises: (i) a DNA sequence and a plasmid replicator mediating
     autonomous replication, wherein the one or more circularized plasmids are
     linearized by digestion of the DNA sequence and removal of a portion of
     the DNA sequence; and (ii) a library of DNA fragments comprising one or
     more mutations of the DNA sequence, wherein the fragments comprise at
     least two regions, one or more regions which are homologous to the 5'
     region or the 3' region of the gap in the linearized DNA sequence and/or
     plasmid sequence and one or more second regions which are homologous to
     the 5' region or the 3' region of the DNA fragments of the library;
     wherein the linearized plasmids and the DNA fragments recombine by in vivo
     recombination to produce a plurality of autonomously replicating plasmids
     comprising one or more variants of the DNA sequence.  In particular,
     disclosed are gene and protein sequences of A. oryzae DNA gap repair genes
     rdhA (rad51 homolog A), rdhB (rad52 homolog) and rdhD (MUS-25 homolog),
     which allow the shuffling of DNA fragments that are homologous with a DNA
     sequence of interest and the recovery of the resulting variants of the DNA
     sequence contained in autonomously replicating plasmids.  Overexpression
     of rdhA or rdhB in A. oryzae are shown to increase the efficiency of
     interplasmid recombination (14-26 fold) and stimulate interchromosomal
     recombination.  The gapped plasmid pCW013 expressing Humicola insolens
     cellobiohydrolase gene cbh1 and cbh1 PCR fragment are cotransfected into
     A. oryzae and the gap repaired plasmids express CBHI at levels comparable
     to transformants harboring the circular plasmid pCW013.  The so called
     "gap repair" method is useful to develop strains for preparing and screening
     variants of foreign genes which has com. values.

L10   ANSWER 7 OF 27  BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN    2004-06229  BIOTECHDS
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TI New bone morphogenic protein polypeptides and polynucleotides, useful for diagnosing, preventing, treating or ameliorating a medical condition, e.g. diabetes, dyslipidemia, hypertension, coronary artery disease or neuropathy;
involving vector-mediated gene transfer and expression in host cell for use in gene therapy

AU YOUNG P E; RUBEN S M

PA YOUNG P E; RUBEN S M

PI US 2003224501 4 Dec 2003

AI US 2003-366345 14 Feb 2003

PRAI US 2003-366345 14 Feb 2003; US 2000-190067 17 Mar 2000

DT Patent

LA English

OS WPI: 2004-022075 [02]

AN 2004-06229 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - An isolated bone morphogenic protein polypeptide (I) comprising a first amino acid sequence at least 90% identical to a second amino acid sequence, is new.

DETAILED DESCRIPTION - The second amino acid sequence consists of: (a) any one of 47 sequences of 104-986 amino acids (II), fully defined in the specification, with or without the **signal sequence** ; (b) the amino acid sequence of the polypeptide encoded by cDNA clone HLDOU18 or HHFBT80; (c) the amino acid sequence of the **propeptide** of any one of 24 sequences of 321-986 amino acids, fully defined in the specification; (d) the amino acid sequence of the mature (secreted) polypeptide of (II); or (e) one or more cysteine rich regions of any one of 23 sequences of 104-139 amino acids, fully defined in the specification. INDEPENDENT CLAIMS are included for the following: (1) a method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising determining the presence or amount of expression of (I) in a biological sample, and diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of (I); (2) a method of identifying a binding partner to (I) comprising contacting (I) with a binding partner, and determining whether the binding partner effects an activity of (I); (3) a method of screening for molecules that modify activities of (I) comprising contacting (I) with a compound suspected of having agonist or antagonist activity, and assaying for activity of (I); (4) a method for preventing, treating or ameliorating a medical condition comprising administering to a mammalian subject a therapeutic amount of (I); (5) a method for regulating nutritional partitioning comprising administering to a mammalian subject a therapeutic amount of (I); (6) a method for limiting weight gain comprising administering to a mammalian subject a therapeutic amount of (I); (7) a method for suppressing appetite comprising administering to a mammalian subject a therapeutic amount of (I); (8) a method for reducing fat mass comprising administering to a mammalian subject a therapeutic amount of (I); (9) a method for increasing the sensitivity of a cell to insulin comprising contacting the cell with (I); and (10) a method for increasing glucose uptake by a cell comprising contacting the cell with (I).

WIDER DISCLOSURE - Also disclosed are isolated nucleic acids containing the coding regions of the genes encoding bone morphogenic protein (BMP) polypeptides, vectors, host cells, **antibodies** that bind to BMP polypeptides, and agonists and antagonists of the polypeptides and polynucleotides.

BIOTECHNOLOGY - Preparation: The bone morphogenic protein polypeptide is prepared by recombinant and synthetic methods. Preferred Polypeptide: The polypeptide may also comprise any one of the second amino acid sequences cited above. The first amino acid sequence is at least 95% identical to any of the second amino acid sequences. The polypeptide is a dimer. Preferred Method: In increasing the sensitivity of a cell to insulin, or increasing glucose uptake by a cell, the cell is a skeletal muscle cell, a liver cell or an adipocyte.

ACTIVITY - Antidiabetic; Antilipemic; Hypotensive; Cardiant; Vasotropic; Nephrotropic; Neuroprotective; Anorectic; Hepatotropic; Osteopathic; Antiinflammatory; Cytostatic. No biological data given.

MECHANISM OF ACTION - BMP Agonist; BMP Antagonist; Gene Therapy.

USE - The bone morphogenic protein (BMP) polypeptides and polynucleotides are useful for diagnosing a pathological condition or a susceptibility to a pathological condition in a subject, or for preventing, treating or ameliorating a medical condition, e.g. diabetes, insulin resistance, hyperinsulinemia, hyperglycemia, dyslipidemia, hypertension, coronary artery disease, renal failure, neuropathy, a metabolic disorder, a glucose metabolic disorder, an insulin disorder, an endocrine disorder, obesity, weight loss, or a liver disorder (all claimed), cartilage and bone growth disorder, inflammation, or aberrant cell growth such as liver cancer. The BMP polypeptides and polynucleotides are also useful for regulating nutritional partitioning, limiting weight gain, suppressing appetite, reducing fat mass, increasing the sensitivity of a cell to insulin, or increasing glucose uptake by a cell.

ADMINISTRATION - Dosage of the **antibody** is 0.1-100 (preferably 1-10) mg/kg. The polypeptide is administered at a dose of 0.1-100 mug/kg/day. Administration may be intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, intranasal, epidural, oral, topical, rectal, intraventricular, or intrathecal.

EXAMPLE - A polynucleotide encoding a bone morphogenic protein (BMP) polypeptide was amplified using PCR oligonucleotide primers corresponding to the 5' and 3' ends of the DNA sequence. The pQE-9 vector was digested with BamHI and XbaI and the amplified fragment was ligated into the pQE-9 vector maintaining the reading frame initiated at the bacterial RBS. The ligation mixture was used to transform a selected Escherichia coli strain M15/rep4. Transformants were identified by their ability to grow on LB plates and ampicillin/kanamycin resistant colonies were selected. Plasmid DNA was isolated and confirmed by restriction analysis. Clones containing the desired constructs were grown overnight in liquid culture in LB media supplemented with ampicillin (100 mug/ml) and kanamycin (25 mug/ml). The cells were grown to a desired optical density. Isopropyl-B-D-thiogalacto pyranoside was added to a final concentration of 1 mM. Cells were grown for an extra 3-4 hours, and the cells were harvested by centrifugation. The cell pellet obtained by the centrifugation was solubilized in the chaotropic agent 6 molar guanidine hydrochloride by stirring for 3-4 hours at 4degreesC. The cell debris was removed by centrifugation, and the supernatant containing the BMP polypeptide was loaded onto a nickel-nitrilo-triacetic acid (Ni-NTA) affinity resin column. Proteins with a 6x His tag bind to the Ni-NTA resin with high affinity, and the BMP protein was purified in a simple one-step procedure. (224 pages)

L10 ANSWER 8 OF 27 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-02019 BIOTECHDS
TI Increasing the homologous recombination of a nucleic acid sequence introduced into a filamentous host cell comprises introducing a population of filamentous host cells a first and second nucleic acid sequence;
new method for deletion mutagenesis, gene disruption and strain improvement in filamentous fungus e.g. Acremonium, Aspergillus, Aureobasidium, Cryptococcus, Filabasidium, Fusarium, Gibberella, Humicola, Magnaporthe, Mucor, Myceliophthora, Myrothecium, Neocallimastix, Neurospora, Paecilomyces, Penicillium, Piromyces, Schizophyllum, Talaromyces, Thermoascus, Thielavia, Trichoderma sp., Escherichia coli plasmid pzL1 rdhB6, pZL1 rdhD10
AU HARRIS P; BRODY H
PA NOVOZYMES BIOTECH INC
PI US 2003199037 23 Oct 2003
AI US 2003-420035 21 Apr 2003
PRAI US 2003-420035 21 Apr 2003; US 2002-374639 22 Apr 2002
DT Patent

LA English
OS WPI: 2003-852789 [79]
AN 2004-02019 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - Increasing the homologous recombination of a nucleic acid sequence introduced into a filamentous host cell comprises introducing a population of filamentous fungal host cells a first nucleic acid sequence encoding a recombination protein and a second nucleic acid sequence comprising one or more regions that are homologous with the genome of the filamentous fungal host cell.

DETAILED DESCRIPTION - Increasing the homologous recombination of a nucleic acid sequence introduced into a filamentous host cell comprises: (a) introducing a population of filamentous fungal host cells a first nucleic acid sequence encoding a recombination protein and a second nucleic acid sequence comprising one or more regions that are homologous with the genome of the filamentous fungal host cell, where the recombination protein promotes the recombination of the one or more regions with the corresponding homologous region in the genome of the filamentous fungal host cell to incorporate the second nucleic acid sequence by homologous recombination and the number of host cells comprising the incorporated nucleic acid sequence is increased at least 20% compared to the same population of filamentous fungal host cells without the first nucleic acid; and (b) isolating from the population of filamentous fungal host cells a filamentous fungal cell comprising the incorporated nucleic acid sequence. INDEPENDENT CLAIMS are included for the following: (1) a method for producing a polypeptide in a filamentous fungal cell by cultivating the filamentous fungal cell in a medium suitable for production of the polypeptide; and recovering the polypeptide from the cultivation medium; (2) a polypeptide obtained by the method in (1); (3) a filamentous fungal host cell comprising one or more nucleic acids encoding the recombination protein; (4) a method for deleting or disrupting a gene in a filamentous fungal cell comprising the step of the novel method; (5) the isolated nucleic acid sequence encoding the recombination protein, or having at least one mutation in its sequence.

BIOTECHNOLOGY - Preferred Method: In increasing the homologous recombination of a nucleic acid sequence introduced into a filamentous host cell, the first nucleic acid encoding the recombination protein is selected from a sequence that is at least 70% identical to 2032, 2500, or 2981 bp, fully defined in the specification; encodes a polypeptide that is at least 70% identical to a sequence of 315, 565 or 811 amino acids, fully defined in the specification; a nucleic acid sequence that hybridizes to, or the cDNA sequence contained in the nucleotide sequences cited above; or the subsequence of the above sequences. The second nucleic acid further comprises a gene that encodes a polypeptide or an RNA, a gene disrupted with a third nucleic acid sequence; a partially or fully deleted gene, a regulatory control sequence or a recombinantly manipulated version of a gene native or foreign to the filamentous fungal host cell. The polypeptide is an **antibody**, hormone, enzyme, receptor, or selectable marker. The enzyme is an oxidoreductase, transferase, hydrolase, lyase, isomerase or ligase. The regulatory control sequence is selected from promoter, **signal sequence**, leader, polyadenylation sequence, **propeptide** sequence, consensus translation initiator sequence, signal peptide sequence, and transcription terminator. The disrupted gene is disrupted with a selectable marker gene selected from amds (acetamidase), argB (ornithine carbomoyltransferase), bar (phosphinothricin acetyltransferase), hygB (hygromycin phosphotransferase), niaD (nitrate reductase), pyrG (orotidine-5'-phosphate decarboxylase), sC (sulfate adenyltransferase), and trp (anthranilate synthase), and their equivalents. The one or more regions homologous with the genome of the filamentous fungal cell is a part of a gene native or foreign to the filamentous fungal host cell. The first and/or second nucleic acid sequence is contained in a plasmid, preferably an autonomously

replicating plasmid, or in a linear fragment, when introduced into the filamentous fungal host cell. The first and/or second nucleic acid sequence is introduced into the chromosome or into an autonomously replicating plasmid of the filamentous host cell. The filamentous fungal cell is Acremonium, Aspergillus, Aureobasidum, Cryptococcus, Filabasidium, Fusarium, Gibberella, Humicola, Magnaporthe, Mucor, Myceliophthora, Myrothecium, Neocallimastix, Neurospora, Paecilomyces, Penicillium, Piromyces, Schizophyllum, Talaromyces, Thermoascus, Thielavia, or Trichoderma strain. The gene is a nucleic acid contained in the plasmid pZL1 rdhA13 that is contained in Escherichia coli NRRL B-30503; plasmid pzL1 rdhB6 that is contained in Escherichia coli NRRL B-30504, or plasmid pZL1 rdhD17 that is contained in Escherichia coli NRRL B-30505 and plasmid pZL1 rdhD10 that is contained in Escherichia coli NRRL B-30506. The first nucleic acid sequence is introduced into the filamentous fungal host cell prior to or simultaneously with the second nucleic acid sequence.

USE - The methods are useful for increasing homologous recombination nucleic acid sequence introduced into a filamentous host cell (claimed) for promoting interplasmid, plasmid-chromosomal, intrachromosomal or interchromosomal recombination. (57 pages)

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L10  ANSWER 9 OF 27  CAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 3
AN   2003:275903  CAPLUS
DN   139:112414
TI   Identification and Characterization of ADAMTS-20 Defines a Novel Subfamily
     of Metalloproteinases-Disintegrins with Multiple Thrombospondin-1 Repeats
     and a Unique GON Domain
AU   Llamazares, Maria; Cal, Santiago; Quesada, Victor; Lopez-Otin, Carlos
CS   Instituto Universitario de Oncologia, Facultad de Medicina, Departamento
     de Bioquimica y Biologia Molecular, Universidad de Oviedo, Oviedo, 33006,
     Spain
SO   Journal of Biological Chemistry (2003), 278(15), 13382-13389
     CODEN: JBCHA3; ISSN: 0021-9258
PB   American Society for Biochemistry and Molecular Biology
DT   Journal
LA   English
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AB We have cloned a mouse brain cDNA encoding a new protein of the ADAMTS family (a disintegrin and metalloproteinase domain, with thrombospondin type-1 repeats), which has been called ADAMTS-20. This protein shows a domain organization similar to that described for other ADAMTSs including **signal sequence**, **propeptide**, metalloproteinase domain, disintegrin domain, central TS-1 motif, cysteine-rich region, and C-terminal TS module. However, this last module is more complex than that of other ADAMTSs, being composed of a total of 14 repeats. The structural complexity of ADAMTS-20 is further increased by the presence of an addnl. domain 200 residues long and located immediately adjacent to the TS module. This domain has been tentatively called GON domain and can also be recognized in some ADAMTSs such as gon-1 from Caenorhabditis elegans and human and mouse ADAMTS-9. The presence of this domain is a hallmark of a novel subfamily of structurally and evolutionarily related ADAMTSs, called GON-ADAMTSs. Expression anal. demonstrated that ADAMTS-20 transcripts can be detected at low levels in several human and mouse tissues, especially in testis. This gene is also overexpressed in some human malignant tumors, including brain, colon, and breast carcinomas. Western blot anal. using polyclonal **antibodies** raised against recombinant ADAMTS-20 produced in Escherichia coli showed the presence of a 70-kDa band in mouse brain and testis exts. This recombinant ADAMTS-20 hydrolyzed a synthetic peptide used for assaying matrix metalloproteinases. These data suggest that this novel enzyme may play a role in the tissue remodeling process occurring in both normal and pathol. conditions.

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RE.CNT  41     THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT
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L10   ANSWER 10 OF 27  BIOTECHNO  COPYRIGHT 2006 Elsevier Science B.V. on STN
      DUPLICATE
AN    2003:36134274   BIOTECHNO
TI    Molecular analysis of Pseudomonas aeruginosa protease IV expressed in
      Pseudomonas putida
AU    Traidej M.; Caballero A.R.; Marquart M.E.; Thibodeaux B.A.; O'Callaghan
      R.J.
CS    R.J. O'Callaghan, Department of Microbiology, LSU Health Sciences Center,
      1901 Perdido Street, New Orleans, LA 70112, United States.
      E-mail: rocall@lsuhsc.edu
SO    Investigative Ophthalmology and Visual Science, (01 JAN 2003), 44/1
      (190-196), 25 reference(s)
      CODEN: IOVSDA  ISSN: 0146-0404
DT    Journal; Article
CY    United States
LA    English
SL    English
AB    PURPOSE. In this study, the protease IV gene of Pseudomonas aeruginosa
      was expressed in the nonocular pathogenic host, Pseudomonas putida, to
      elucidate the molecular properties and virulence contribution of the
      enzyme. Recent determination of the protease IV gene sequence suggests
      that the protein of 463 amino acids contains a signal
      sequence, a propeptide domain, and a mature protease.
      The only form of this protein that has been detected previously is the
      extracellular mature protease. METHODS. The protease IV gene was cloned
      and expressed in a protease IV-negative Pseudomonas species, P. putida.
      The cloned protease IV gene product was analyzed to identify biochemical,
      enzymatic, and immunologic properties and its contribution to corneal
      virulence. RESULTS. P. putida expressing the cloned protease IV gene had
      significantly greater extracellular enzyme activity than P. aeruginosa.
      These P. putida cell extracts produced a protein with the same molecular
      mass as mature protease IV and two other polypeptides representing larger
      precursors, all of which were recognized by protease IV-specific
      antibodies. P. putida producing protease IV, relative to P.
      putida with the vector alone, caused a threefold increase in ocular
      inflammation and tissue damage when intrastromally injected into rabbit
      corneas. CONCLUSIONS. The present study demonstrates for the first time
      that protease IV is synthesized as a large precursor that is processed
      intracellularly through an intermediate form and secreted into the
      extracellular milieu as a mature protease. The results also confirm a
      significant correlation between production of protease IV and corneal
      virulence.

L10  ANSWER 11 OF 27  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2002:937303  CAPLUS
DN   138:20443
TI   Endocrine disruptor screening using DNA chips of endocrine
     disruptor-responsive genes
IN   Kondo, Akihiro; Takeda, Takeshi; Mizutani, Shigetoshi; Tsujimoto,
     Yoshimasa; Takashima, Ryokichi; Enoki, Yuki; Kato, Ikunoshin
PA   Takara Bio Inc., Japan
SO   Jpn. Kokai Tokkyo Koho, 386 pp.
     CODEN: JKXXAF
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   JP 2002355079        A2    20021210    JP 2002-69354          20020313
PRAI JP 2001-73183        A     20010314
     JP 2001-74993        A     20010315
     JP 2001-102519       A     20010330
AB   A method and kit for detecting endocrine-disrupting chems. using DNA
     microarrays are claimed.  The method comprises preparing a nucleic acid
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sample containing mRNAs or cDNAs originating in cells, tissues, or organisms which have been brought into contact with a sample containing the endocrine disruptor. The nucleic acid sample is hybridized with DNA microarrays having genes affected by the endocrine disruptor or DNA fragments originating in these genes have been fixed. The results obtained are then compared with the results obtained with the control sample to select the gene affected by the endocrine disruptor. Genes whose expression is altered by tri-Bu tin, 4-octaphenol, 4-nonylphenol, di-N-Bu phthalate, dichlorohexyl phthalate, octachlorostyrene, benzophenone, diethylhexyl phthalate, diethylstilbestrol (DES), and 17-β estradiol (E2), were found in mice by DNA chip anal.

L10 ANSWER 12 OF 27 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2002-19970 BIOTECHDS
TI Tissue-specific secretory protein expression product of gene DRL138, useful for diagnosis treatment and prevention of cancer and other diseases associated with its expression;
vector-mediated neomycin-resistance reporter gene transfer and expression in host cell, transgenic mouse and transgenic rat construction for disease diagnosis and gene therapy
AU ITO Y; MOGI S
PA TAKEDA CHEM IND LTD
PI WO 2002050270 27 Jun 2002
AI WO 2000-JP11080 19 Dec 2000
PRAI JP 2000-385192 19 Dec 2000
DT Patent
LA Japanese
OS WPI: 2002-537701 [57]
AN 2002-19970 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - Human and mouse polypeptides comprising sequences fully defined in the specification, which are the expression products of gene DRL138, including the mature polypeptide, its **propeptide**, and **propeptide** with **signal sequence** at the N-terminal, along with their amide, ester and salt derivatives, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) peptides containing partial sequences of (I); (2) polynucleotides encoding (I); (3) expression vectors containing the polynucleotides; (4) host cells transformed by the vectors; (5) production of (I) by culture of the transformed cells; (6) **antibodies** recognizing all or part of (I); (7) screening potential promoters and inhibitors of the activity of (I) by contacting with (I) or cells expressing it and selecting for modification of activity; (8) kits for the screening method; (9) compounds identified by the screening method; (10) drug compositions containing these compounds, or containing (I) or **antibodies** to (I) or polynucleotides encoding (I); (11) diagnostic agents containing **antibodies** to (I); (12) antisense DNA to DNA encoding all or part of (I), and drug compositions and diagnostic agents containing this antisense DNA; (13) transgenic non-human animals transformed by DNA encoding (I); (14) expression vectors containing DNA encoding (I) or modified forms of it, for use in expression in non-human animals; (15) stem cells from non-human animals in which DRL138 gene has been inactivated and a reporter gene inserted; (16) knockout animals for the DRL138 gene; and (17) screening compounds for promotion or inhibition of the DRL138 gene, using these knockout animals.

BIOTECHNOLOGY - Preferred Transgenic Animal: Transgenic animals and knockout animals are preferably rodents, such as mice or rats. Preferred Reporter Gene: The reporter gene used in the transformed stem cells is a neomycin resistance gene. Preferred Polypeptide: Recombinant polypeptide may be tagged with a C-terminal FLAG sequence.

ACTIVITY - Cytostatic; Vasotropic; Immunomodulatory; Antibacterial; Antiarthritic; Antiinflammatory; Respiratory general; Hormonal general; Osteopathic.

MECHANISM OF ACTION - (I) is a secretory polypeptide expressed in specific tissues.

USE - Treatment, prevention and diagnosis of respiratory disease, cancer, immune disorders, infection, digestive disorders, circulatory diseases, endocrine disorders, bone diseases and arthritis.

EXAMPLE - The human genome database was searched for potential open reading frames (ORF) encoding polypeptides having a secretory **signal sequence** and basic amino acid pairs (such as Arg-Arg or Lys-Arg). A new ORF was identified originating in chromosome 10, and primers devised and synthesized for its amplification from a human multiple-tissue cDNA panel (Clontech K1421-1). A 0.5 kb fragment was obtained and sequenced (DRL138 cDNA). (100 pages)

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L10  ANSWER 13 OF 27  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2001:781079  CAPLUS
DN   135:348851
TI   Albumin fusion proteins with therapeutic proteins for improved shelf-life
IN   Rosen, Craig A.; Haseltine, William A.
PA   Human Genome Sciences, Inc, USA
SO   PCT Int. Appl., 606 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 8
     PATENT NO.          KIND  DATE        APPLICATION NO.        DATE
     ---------------     ----  --------    --------------------   --------
PI   WO 2001079444        A2   20011025    WO 2001-US12013        20010412
     WO 2001079444        A3   20020523
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
             VN, YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 2001074809        A5   20011020    AU 2001-74809          20010412
     CA 2405557           AA   20011025    CA 2001-2405557        20010412
     EP 1278544           A2   20030129    EP 2001-941457         20010412
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     US 2003125247        A1   20030703    US 2001-833041         20010412
     US 6994857           B2   20060207
     US 2003171267        A1   20030911    US 2001-833117         20010412
     JP 2003530847        T2   20031021    JP 2001-577428         20010412
     US 2003199043        A1   20031023    US 2001-832501         20010412
     US 2003219875        A1   20031127    US 2001-833118         20010412
     US 6905688           B2   20050614
     US 2004010134        A1   20040115    US 2001-833245         20010412
     US 6946134           B1   20050920    US 2001-833111         20010412
     US 2005100991        A1   20050512    US 2004-932104         20040902
     US 2005244931        A1   20051103    US 2004-967457         20041019
     US 2005266532        A1   20051201    US 2005-78663          20050314
     US 2005266533        A1   20051201    US 2005-78914          20050314
     US 2006084794        A1   20060420    US 2005-264096         20051102
PRAI US 2000-229358P      P    20000412
     US 2000-199384P      P    20000425
     US 2000-256931P      P    20001221
     US 2001-832501       B1   20010412
     US 2001-833041       A3   20010412
     US 2001-833117       B1   20010412
     US 2001-833118       A3   20010412
     US 2001-833245       A3   20010412
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WO 2001-US12013 W 20010412

AB The present invention encompasses fusion proteins of albumin with various therapeutic proteins. Therapeutic proteins may be stabilized to extend the shelf-life, and/or to retain the therapeutic protein's activity for extended periods of time in solution, in vitro and/or in vivo, by genetically or chemical fusing or conjugating the therapeutic protein to albumin or a fragment or variant of albumin. Use of albumin fusion proteins may also reduce the need to formulate the protein solns. with large excesses of carrier proteins to prevent loss of therapeutic proteins due to factors such as binding to the container. Nucleic acid mols. encoding the albumin fusion proteins of the invention are also encompassed by the invention, as are vectors containing these nucleic acids, host cells transformed with these nucleic acids vectors, and methods of making the albumin fusion proteins of the invention and using these nucleic acids, vectors, and/or host cells. Thus, plasmid vectors are constructed in which DNA encoding the desired therapeutic protein may be inserted for expression of the albumin fusion proteins in yeast (pPPC0005) and mammalian cells (pC4:HSA). Yeast-derived **signal sequences** from Saccharomyces cerevisiae invertase SUC2 gene, or the stanniocalcin or native human serum albumin signal peptides, are used for secretion in yeast or mammalian systems, resp. Thus, the fusion product of human growth hormone with residues 1-387 of human serum albumin retains essentially intact biol. activity after 5 wk of incubation in tissue culture media at 37°, whereas recombinant human growth hormone used as control lost its biol. activity in the first week. Although the potency of the albumin fusion proteins is slightly lower than the unfused counterparts in rapid bioassays, their biol. stability results in much higher biol. activity in the longer term in vitro assay or in vivo assays. Addnl., the present invention encompasses pharmaceutical compns. comprising albumin fusion proteins and methods of treating, preventing, or ameliorating diseases, disorders or conditions using albumin fusion proteins of the invention.

L10 ANSWER 14 OF 27 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN

AN 2002-05639 BIOTECHDS

TI Novel purified human eosinophil serine protease 1-like enzyme, useful for identifying modulators of enzyme activity for treating Paget's disease, osteoporosis, airway allergy, asthma;
involving vector-mediated gene transfer for expression in host cell, for use in drug screening and disease diagnosis and therapy

AU XIAO Y

PA BAYER AG

PI WO 2001098503 27 Dec 2001

AI WO 2000-EP6936 21 Jun 2000

PRAI US 2001-279766 30 Mar 2001

DT Patent

LA English

OS WPI: 2002-122283 [16]

AN 2002-05639 BIOTECHDS

AB DERWENT ABSTRACT:
NOVELTY - A purified human eosinophil serine protease (esp) 1-like enzyme (I) having a a 339, 279, 334, 305 or 259 residue amino acid sequence, fully defined in the specification, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) an isolated polynucleotide (II): (a) encoding (I) which comprises an amino acid sequence of PS or an amino acid sequence which is at least 52 % identical to PS; (b) comprising a 1018 (S1) or 837 (S8) nucleotide sequence, fully defined in the specification; (c) which hybridizes under stringent conditions to an above mentioned polynucleotide; (d) having a sequence which deviates from the above mentioned sequences due to degeneracy of genetic code; or (e) which represents a fragment, derivative or allelic variant of the above mentioned polynucleotide sequences; (2) an expression vector (III) containing (II); (3) a host cell (IV) containing (III); (4) a substantially purified esp 1-like polypeptide (P1) encoded by (II); (5)

preparation of (I), comprising culturing (IV) under expression conditions, and recovering the polypeptide; (6) a reagent (V) that modulates the activity of (I) or (II), which is identified by screening methods involving (P1) or (I), or (II); (7) a diagnostic kit for detecting a coding sequence for a polypeptide comprising an amino acid sequence of PS, comprising a polynucleotide having 11 contiguous nucleotides of (S1) or (S8) and instructions of carrying out the detection method; (8) a kit for detecting a polypeptide comprising an amino acid sequence of PS, comprising an **antibody** which specifically binds to (I) and instructions for carrying out the method; (9) a pharmaceutical composition (VI) comprising (III) or (V) which specifically binds to (I) having an amino acid sequence of PS, or to (II) and modulates their activity, identified by screening methods involving (P1) or (I), or (II); and a carrier; (10) a fusion protein comprising (I); (11) screening (M1) for agents which modulate an activity of a human esp 1-like enzyme comprising contacting a test compound with a product encoded by a polynucleotide which comprises the nucleotide sequence of (S1) or (S8) and detecting binding of the test compound of the product, where a test compound which binds to the product is identified as a potential agent for regulating the activity of the human esp 1-like enzyme; (12) reducing (M2) activity of human esp 1-like enzyme comprising contacting a cell with a reagent which specifically binds to a product encoded by a polynucleotide comprising the nucleotide sequence of (S1) or (S8); and (13) a pharmaceutical composition comprising a reagent which binds to a product of a polynucleotide comprising the nucleotide sequence of (S1) or (S8) and a carrier.

WIDER DISCLOSURE - **Antibodies** against (I) are disclosed as new.

BIOTECHNOLOGY - Preferred Polynucleotide: (II) is a cDNA molecule having a sequence of (S1) or (S8), and encoding an amino acid sequence of PS. Preferred Polypeptide: (I) consists of an amino acid sequence of PS. Preferred Method: The product encoded by (II) which is contacted with test compound is a polypeptide or RNA. In (M2), if the product is polypeptide, then the reagent employed for reducing the activity of human esp 1-like enzyme is an **antibody**, and if the product is an RNA, then the reagent used is ribozyme or an antisense oligonucleotide. The reagent is contacted with cell in vivo or in vitro.

ACTIVITY - Antiinflammatory; antiasthmatic; antiallergic; osteopathic; cytostatic; dermatological. Synthesis of an antisense esp 1-like enzyme oligonucleotide comprising at least 11 contiguous nucleotides from the complement of a 1018 nucleotide sequence, fully in the specification was performed on a Pharmacia Gene Assembler series synthesizer. Following assembly and deprotection, the oligonucleotide was twice ethanol-precipitated, dried and suspended in phosphate-buffered saline (PBS) at the desired concentration. Purity of the oligonucleotides was tested by capillary gel electrophoresis and ion exchange high performance liquid chromatography (HPLC). The endotoxin level in the oligonucleotide preparation was determined using the Limulus Amebocyte assay. An aqueous composition containing the antisense oligonucleotide at a concentration of 0.1-100 micro-m was administered directly to a patient having asthma by injection. The severity of the patient's asthma was decreased.

MECHANISM OF ACTION - esp 1-like enzyme activity modulator.

USE - (I) is useful for screening for agents which decrease the activity of an esp 1-like enzyme which involves contacting a test compound with (P1) or (II), and detecting binding of test compound to polypeptide or polynucleotide. The test compound which binds to the polypeptide or polynucleotide is identified as a potential therapeutic agent for decreasing the activity of esp 1-like enzyme. (I) is also useful for screening for agents which regulate the activity of an esp 1-like enzyme. The method involves contacting a test compound with (P1) or (I) and detecting the esp 1-like enzyme activity of the polypeptide. The test compound which increases or decreases the esp 1-like enzyme activity is identified as a potential therapeutic for increasing or decreasing the esp 1-like enzyme activity. The method optionally involves detecting binding of the test compound to the polypeptide and a test compound which binds to the polypeptide is identified as a potential agent for regulating activity of the human esp 1-like enzyme. The polypeptide is contacted with the test compound in a cell, in vitro or in a cell-free system. Either the polypeptide or the test compound comprises a detectable label and the test compound when binding to the polypeptide displaces the labeled ligand bound to the polypeptide. Also, the polypeptide or the test compound is bound to a solid support. (II) is useful for detecting a polynucleotide which encodes (I) in a biological sample which involves hybridizing a polynucleotide comprising 11 contiguous nucleotides of (S1) or (S8) to a nucleic acid material of a biological sample, thereby forming a hybridization complex and detecting a hybridization complex. Before hybridization the nucleic acid material of the biological sample is amplified. (V) is useful for detecting (P1) or (II) which involves contacting a biological sample with (V). (V) is also useful for reducing the activity of esp 1-like enzyme which involves contacting a cell with (V) which binds to (II) or (P1). (V) (an **antibody** is useful for detecting the polypeptide having an amino acid sequence of PS. (V) is also useful for treating a esp 1-like enzyme dysfunction related diseases condition such as asthma, chronic obstructive pulmonary disease, airway allergy or osteoporosis. (VI) is useful for modulating esp 1-like enzyme activity in a disease condition as mentioned above. (All claimed). (I) is useful in diagnostic assays for detecting diseases and abnormalities or susceptibility to diseases and abnormalities related to presence of mutations in the nucleic acid sequences which encode the enzyme. (V) is also useful for treating dermatitis, Paget's disease, and preventing degradation of bone implants particularly dental implants.

ADMINISTRATION - Pharmaceutical compositions comprising (I), (II) or (V) are administered by oral, intravenous, intramuscular, intraperitoneal, or parenteral route. Dosage of (V) ranges from 0.1-100000 micro-g. In vivo dosages of an **antibody** (i.e. (V)) range from 5-50 micro-g/kg. Polynucleotides encoding single chain **antibodies** are administered in dosages ranging from 100-200 ng.

EXAMPLE - Polymerase chain reaction (PCR) amplification of human eosinophil serine protease (ESP) 1-like enzyme gene from human trachea cDNA library results in 3 PCR products. Cloning and sequence analysis of the three PCR products showed that ESP 1-like enzyme gene has three splicing variants with the sequences slightly different from previously identified. The existence of the splicing variants was confirmed by using primers covering the sequences of splicing junction. ESP 1-like enzyme and its variants, namely ESP-1-L-L, ESP-1-L-M, and ESP-1-L-S, encode polypeptides containing 334, 305 and 259 amino acids, respectively. All these splicing forms contained the triad catalytic domains. However the hydrophobic region of the N-terminal **signal sequence** in ESP 1-L-S was partially deleted, indicating that ESP-1-L-S has a cytoplasmic localization. ESP-1-like enzyme genes have less than 50 % identity with ESP-1, a serine protease identified from eosinophils. High homologies were observed in N-terminal **signal sequence** , three serine protease catalytic domains and a hydrophobic tails. Based on database searches and computer-assisted multiple sequence alignments and phylogenetic comparisons, in addition to the similarity with ESP-1, ESP-1-like enzyme amino acid sequences were most similar to the well-characterized tryptases, such as mouse tryptase 4, human tryptase alpha, beta, gamma and protasin. ESP 1-like enzyme has the particularly tryptic-like serine protease structure features, e.g. the catalytic triad residue His (94 for ESP-1-L-L), Asp (163 for ESP-1-L-L) and Ser (265 for ESP-1-L-L). Features shared with tryptase gamma, prostatin and ESP-1 include Cys62 and Cys183. However, the ending of the Arg of a **propeptide** was not existed in ESP 1-like. In addition, LeuProProProTyr motif for oligomerization identified in tryptase beta is conserved in the ESP-1-like enzyme. Therefore both mechanisms involved in activation of tryptase-like serine proteases are employed by ESP-1-like enzyme. ESP-1-like enzyme was expressed as a membrane protease and expression of ESP-1-like enzyme induces protease activity in membrane fraction. Recombinant ESP-1-like-enzyme-V5-His was expressed in A549 cells. Immunostaining of A549 cells and immunoblotting of fractional cell lysates with anti-V5 **antibodies** showed that ESP 1-like enzyme was expressed as a membrane protein. When the membrane fractions from ESP 1-like enzyme expressing A549 cells were subjected to protease assay with a panel of peptide structures, cleavages were observed with the following peptides. Suc-Ala-Ala-Pro-Phe-MCA (chymotrypsin), Pro-Phe-Arg-MCA (Kallikrein), Boc-Glu-Ala-Arg-MCA (Trypsin) and Boc-Phe-Ser-Arg-MCA (Tryptase). These substrates were not active with the membrane fractions prepared from A549 cells transfected with the mock vectors. Therefore, the protease activities in the membrane fraction of ESP-1-like enzyme expressing A549 cells were contributed either directly by ESP-1-like enzyme itself or by ESP-1-like-activated proteases. Further experiment carried out showed that ESP-1-like enzyme is secreted from cells after proteolysis in the inflammed tissue and functions as inflammatory mediators involving in airway damage and remodeling. Greatly increased expression of ESP-1-like enzyme was bronchial endothelial cells by interleukin (IL)-4, CD40 and tumor necrosis factor (TNF)-alpha stimulation showed that ESP-1-like enzyme serine protease plays pivotal roles in inflammation-induced endothelium leakage, plasma exudation, mucus production, tissue swelling, and infiltration of leukocytes. The induced expression was also observed in bronchial epithelial cells, indicating that ESP-1-like enzyme may involve in damaging and shedding of epithelium. (131 pages)

L10 ANSWER 15 OF 27 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
AN 2001:32222419 BIOTECHNO
TI Nuclear forms of parathyroid hormone-related peptide are translated from non-AUG start sites downstream from the initiator methionine
AU Audrey Nguyen M.T.; He B.; Karaplis A.C.
CS A.C. Karaplis, Lady Davis Inst. for Med. Research, 3755 Cote-Ste-Catherine Road, Montreal, Que., Canada.
E-mail: akarapli@ldi.jgh.mcgill.ca
SO Endocrinology, (2001), 142/2 (694-703), 49 reference(s)
CODEN: ENDOAO ISSN: 0013-7227
DT Journal; Article
CY United States
LA English
SL English
AB PTH-related peptide (PTHrP), normally a secreted protein, exerts at least part of its biological functions via intracrine actions at the level of the cell nucleus/nucleolus. To gain insight into the mechanism whereby this peptide accesses the cytosol for subsequent nuclear import, we characterized its nuclear forms. In transfected COS-1 cells, three nuclear PTHrP species were produced, which were larger than the mature form of the protein but smaller than prepro-PTHrP and comprised both the amino- and carboxyl-terminal regions of the peptide. This suggested that nuclear PTHrP proteins contain part of the prepropeptide and likely arise from alternate initiation of translation at downstream non-AUG codons within the **signal sequence**. Transient expression of two PTHrP forms, one in which the unique initiator ATG was mutated to a noninitiator ATC codon, and another encompassing an engineered N-linked glycosylation site, generated peptides of size comparable to nuclear PTHrP proteins. These were inefficiently targeted to the ER, bypassed ER transit, and exclusively localized to nucleoli. Using a polyclonal antiserum against the proregion of PTHrP, nuclear PTHrP species were shown to harbor the **propeptide** sequence. Hence, our data argue that nuclear PTHrP forms result from translation initiated at alternate, internal codons. This may constitute the first example of translation initiation at downstream non-AUG codons in a mammalian protein.

L10 ANSWER 16 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5

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AN    2001:866197  CAPLUS
DN    137:2262
TI    High expression of 92 kDa type IV collagenase (matrix metalloproteinase-9)
      in canine mammary adenocarcinoma
AU    Yokota, Hiroshi; Kumata, Tsuyoshi; Taketaba, Sachiyo; Kobayashi, Tsutomu;
      Moue, Hitoshi; Taniyama, Hiroyuki; Hirayama, Kazuko; Yumiko, Kagawa; Itoh,
      Noboru; Fujita, Osamu; Nakade, Tetsuya; Yuasa, Akira
CS    Department of Veterinary Biochemistry, School of Veterinary Medicine,
      Rakuno Gakuen University, Ebetsu, Hokkaido, 069-8501, Japan
SO    Biochimica et Biophysica Acta, General Subjects (2001), 1568(1), 7-12
      CODEN: BBGSB3; ISSN: 0304-4165
PB    Elsevier B.V.
DT    Journal
LA    English
AB    The 92 kDa type VI collagenase (matrix metalloproteinase-9 (MMP-9))
      activities on zymog. assay were found to be 1-6 times higher in benign
      tumor breast tissues of 12 canines and 4-26 times higher in adenocarcinoma
      breast tissues of nine canines than that of control tissues, resp.  A
      full-length canine MMP-9 cDNA was cloned from the adenocarcinoma tissue by
      reverse transcription-PCR and 5'- and 3'-RACE.  The isolated cDNA
      contained an open reading frame coding for a polypeptide of 704 amino
      acids.  The predicted protein sequence displayed extensive similarity to
      that of known MMP-9s and contained a putative signal
      sequence, a propeptide, an active site with three
      zinc-binding histidine residues, a calcium-binding domain, a hemopexin
      region, and three key cysteine residues.  Western blotting using
      MMP-9-specific antibodies prepared against the peptide
      corresponding to Arg642-Asp704 of canine MMP-9 and Northern blotting using
      a MMP-9-specific cDNA fragment as a probe confirmed that MMP-9 (the 92 kDa
      protein band) was highly expressed in canine mammary adenocarcinoma
      tissues.  Higher levels of MMP-9 activity were found in the sera of
      canines with mammary adenocarcinoma.  The results indicated that MMP-9
      plays an important role in the progression of a canine mammary tumor and
      that assay of serum MMP-9 is helpful for early diagnosis as progress of
      adenocarcinoma.
RE.CNT  19     THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
               ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10   ANSWER 17 OF 27  CAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 6
AN    1997:622360  CAPLUS
DN    127:305331
TI    Proteinase A, a storage-globulin-degrading endopeptidase of vetch (Vicia
      sativa L.) seeds, is not involved in early steps of storage-protein
      mobilization
AU    Becker, Claudia; Senyuk, Vitalyi I.; Shutov, Andrei D.; Nong, Van Hai;
      Fischer, Jurgen; Horstmann, Christian; Kuntz, Klaus
CS    Institut fur Pflanzengenetik und Kulturpflanzenforschung, Gatersleben,
      D-06466, Germany
SO    European Journal of Biochemistry (1997), 248(2), 304-312
      CODEN: EJBCAI; ISSN: 0014-2956
PB    Springer
DT    Journal
LA    English
AB    Proteinase A is a papain-like cysteine endopeptidase of vetch (Vicia
      sativa L.) which was assumed to initiate storage-globulin breakdown just
      after the onset of seed germination.  This enzyme was purified from
      cotyledons of vetch seedlings.  On gelatin-containing SDS gels, active
      proteinase A migrated with an apparent mol. mass of 21 kDa, whereas after
      heat denaturation its mol. size on SDS/PAGE was 29 kDa.  Although
      proteinase A is capable of hydrolyzing storage globulins in vitro it could
      not be localized in the protein-body fraction of cotyledons from
      germinating seeds.  CDNA clones encoding proteinase A precursor have been
      obtained by PCR.  The precursor is composed of an N-terminal
      signal sequence followed by a propeptide, the
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region encoding mature proteinase A, and a C-terminal KDEL sequence. Mature proteinase A with a derived mol. mass of 25,244 Da does not have the KDEL sequence. The derived amino acid sequence of the proteinase A precursor is 78.2% identical to sulfhydryl-endopeptidase (SH-EP), a cysteine endopeptidase from germinating Vigna mungo seedlings. Northern blot anal. indicated that proteinase A mRNA appears de novo in cotyledons of 1-day-germinated vetch seeds, where its amount increases up to day 6. No proteinase A mRNA was detected in other vetch organs, not even in the embryo axis, which contains stored globulins. By means of **antibodies** raised against the purified and against recombinantly produced proteinase A, the 29-kDa bands of mature proteinase A were detected in cotyledon exts. of 6-day-germinated seeds when globulin degradation has already far proceeded. The reported data do not agree with the proposed triggering role of proteinase A in storage-globulin breakdown during germination.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 18 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7
AN 1996:288994 CAPLUS
DN 125:28980
TI Acetyl xylan esterase from Trichoderma reesei contains an active-site serine residue and a cellulose-binding domain
AU Margolles-Clark, Emilio; Tenkanen, Maija; Soederlund, Hans; Penttilae, Merja
CS VTT Biotechnology and Food Research, Espoo, FIN-02044, Finland
SO European Journal of Biochemistry (1996), 237(3), 553-560
CODEN: EJBCAI; ISSN: 0014-2956
PB Springer
DT Journal
LA English
AB The axel gene encoding acetyl xylan esterase was isolated from an expression library of the filamentous fungus Trichoderma reesei using **antibodies** raised against the purified enzyme. Apparently, axel codes for the 2 forms, pI 7 and pI 6.8, of acetyl xylan esterase previously characterized. The axel encodes 302 amino acids including a **signal sequence** and a putative **propeptide**.
The catalytic domain has no amino acid similarity with the reported acetyl xylan esterases but has a clear similarity, especially in the active site, with fungal cutinases which are serine esterases. Similarly to serine esterases, the axel product was inactivated with phenylmethylsulfonyl fluoride. At its C-terminus it carries a cellulose binding domain of fungal type, which is separated from the catalytic domain by a region rich in serine, glycine, threonine, and proline. The binding domain can be separated from the catalytic domain by limited proteolysis without affecting the activity of the enzyme towards acetylated xylan, but abolishing its capability to bind cellulose.

L10 ANSWER 19 OF 27 BIOTECHNO COPYRIGHT 2006 Elsevier Science B.V. on STN
AN 1996:26097923 BIOTECHNO
TI Secretion of an enzymatically active Trichoderma harzianum endochitinase by Saccharomyces cerevisiae
AU Draborg H.; Christgau S.; Halkier T.; Rasmussen G.; Dalboge H.; Kauppinen S.
CS GeneSearch, Novo Nordisk A-S, Novo Alle,DK-2880 Bagsvaerd, Denmark.
SO Current Genetics, (1996), 29/4 (404-409)
CODEN: CUGED5 ISSN: 0172-8083
DT Journal; Article
CY Germany, Federal Republic of
LA English
SL English
AB A novel endochitinase agar-plate assay has been developed and used to identify 11 full-length cDNAs encoding endochitinase I (ENC I) from a Trichoderma harzianum cDNA library by expression in yeast. The 1473-bp

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      chi1 cDNA encodes a 424-residue precursor protein including both a
      signal sequence and a propeptide. The deduced
      ENC I amino-acid sequence is homologous to other fungal and bacterial
      chitinases, and the enzyme cross-reacts with a polyclonal antiserum
      raised against chitinase A1 from Bacillus circulans. The T. harzianum
      endochitinase I was secreted into the culture medium by the yeast
      Saccharomyces cerevisiae in a functionally active form. The purified
      recombinant enzyme had a molecular mass of 44 kDa, an isoelectric point
      of 6.3, a pH optimum of 7.0 and a temperature optimum of 20°C.

L10  ANSWER 20 OF 27  CAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 8
AN   1993:536198  CAPLUS
DN   119:136198
TI   Cell type-specific regulation of SL-1 and SL-2 genes. Induction of the
     SL-2 gene but not the SL-1 gene by human keratinocytes in response to
     cytokines and phorbol esters
AU   Windsor, L. Jack; Grenett, Hernan; Birkedal-Hansen, Bente; Bodden, M.
     Kirby; Engler, Jeffrey A.; Birkedal-Hansen, Henning
CS   Sch. Dent., Univ. Alabama, Birmingham, AL, USA
SO   Journal of Biological Chemistry (1993), 268(23), 17341-7
     CODEN: JBCHA3; ISSN: 0021-9258
DT   Journal
LA   English
AB   The stromelysin-2 (SL-2) gene is transcriptionally active in normal human
     keratinocytes and encodes a secreted, catalytically competent but latent
     matrix metalloproteinase.  Phorbol ester induction resulted in the
     emergence of SL-2 (but not SL-1 transcripts), whereas the opposite was
     true for human mucosal fibroblasts.  Expression of keratinocyte SL-2 was
     also induced by the two keratinocyte growth factors, transforming growth
     factor-α and epidermal growth factor, by the proinflammatory
     cytokine, tumor necrosis factor-α, but, somewhat surprisingly, not
     by interleukin-1β.  The latent SL-2 proenzyme was isolated from
     12-O-tetradecanoylphorbol-13-acetate-induced keratinocytes by
     immunoaffinity chromatog. using a cross-reactive antibody raised
     against human SL-1.  This procedure led to the recovery of a single Mr
     54,000 mol. species at a level of ≈0.2 μg/mL of culture medium.
     Amino-terminal sequencing identified the protein as SL-2 and verified the
     predicted signal sequence cleavage site.
     Conformational activation of latent SL-2 precursor by SDS gave rise to a
     full-length, uncleaved (Mr 54,000) active form and at the same time
     exposed a cryptic thiol group.  By contrast, organomercurial activation
     resulted in autolytic truncation of the mol. with loss of Mr
     ≈10,000  propeptide.  SL-2 shared with (human fibroblast)
     SL-1 the ability to cleave casein, to "superactivate" fibroblast-type
     procollagenase, and to form apparently binary, SDS-resistant complexes
     with tissue inhibitor of metalloproteinases-1.

L10   ANSWER 21 OF 27  BIOTECHNO  COPYRIGHT 2006 Elsevier Science B.V. on STN
AN    1993:23349055   BIOTECHNO
TI    A novel dysfunctional protein C (Protein C Padua 2) associated with a
      thrombotic tendency: Substitution of Cys for Arg-1 results in a strongly
      reduced affinity for binding of Ca.sup.+.sup.+
AU    Girolami A.; Simioni P.; Girolami B.; Marchiori A.; Millar D.S.; Bignell
      P.; Kakkar V.V.; Cooper D.N.
CS    Institute of Medical Semeiotics, IV Chair of Internal Medicine,
      University of Padua Medical School, Via Ospedale 105,35100 Padua, Italy.
SO    British Journal of Haematology, (1993), 85/3 (521-527)
      CODEN: BJHEAL  ISSN: 0007-1048
DT    Journal; Article
CY    United Kingdom
LA    English
SL    English
AB    A dysfunctional protein C (PC) molecule (Protein C Padua 2) was found in
      a 40-year-old man presenting with recurrent deep vein
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thrombosis/pulmonary embolism and a family history of thrombotic disease. The patient exhibited a normal PC antigen level, normal chromogenic activity (using Protac as PC activator) but markedly reduced coagulometric activity. After adsorption of patient plasma onto Al(OH).sub.3, between 30% and 45% PC antigen/chromogenic activity but no coagulometric activity was detectable in the supernatant. The dysfunctional molecule exhibited reduced affinity for a Ca.sup.+.sup.+ dependent anti-protein C monoclonal **antibody** as detected by specific ELISA assay. Immunoblotting experiments showed that PC Padua 2 had an increased MW (95 kD v 65 kD for normal PC). The lesion responsible was determined by PCR/direct sequencing to be a heterozygous CGT/TGT transition in exon 3 of the protein C gene resulting in the substitution of Arg by Cys at residue -1 in the pro-peptide **leader sequence**. The presence of a high MW PC was consistent with the fact that (part of) the **propeptide** (at least Cys-1) still was attached to the protein C molecule. This finding could also explain the strongly reduced affinity of PC Padua 2 for the Ca.sup.+.sup.+ dependent anti-protein C monoclonals.

L10 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1992:422274 CAPLUS
DN 117:22274
TI Expression of active horseradish peroxidase in Saccharomyces cerevisiae
AU Vlamis-Gardikas, Alexios; Smith, Andrew T.; Clements, John M.; Burke, Julian F.
CS Dep. Biochem., Univ. Sussex, Brighton, BN1 9QG, UK
SO Biochemical Society Transactions (1992), 20(2), 111S
CODEN: BCSTB5; ISSN: 0300-5127
DT Journal
LA English
AB Horseradish peroxidase (HRP) was expressed in yeast cells, purified, and characterized. For expression, a HRP construct was made containing the C-terminal prepeptide fused downstream from the HRP synthetic gene. The synthetic gene was fused in-frame to the prepro α-factor **leader sequence** in order to direct extracellular secretion, and the plasmid was replicated in a S. cerevisiae culture. Recombinant HRP was purified from the culture fluid using chromatog. The purified enzyme was deglycosylated and the deglycosylated form cross-reacted with HRP **antibodies**. Thus, the recombinant enzyme is secreted in the normal form, e.g. in a hyperglycosylated state with the C-terminal **propeptide** removed.

L10 ANSWER 23 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 9
AN 1991:577596 CAPLUS
DN 115:177596
TI Co- and post-translational processing of the hevein preproprotein of latex of the rubber tree (Hevea brasiliensis)
AU Lee, Hyung I.; Broekaert, Willem F.; Raikhel, Natasha V.
CS Dep. Energy, Michigan State Univ., East Lansing, MI, 48824-1312, USA
SO Journal of Biological Chemistry (1991), 266(24), 15944-8
CODEN: JBCHA3; ISSN: 0021-9258
DT Journal
LA English
AB Hevein is a chitin-binding protein of 43 amino acids found in the lutoid body-enriched fraction of rubber tree latex. A hevein cDNA clone (HEV1) (Broekaert, W., et al. 1990) encodes a putative **signal sequence** of 17 amino acids followed by a polypeptide of 187 amino acids. Interestingly, this polypeptide has two distinct domains: an amino-terminal domain of 43 amino acids, corresponding to mature hevein, and a carboxyl-terminal domain of 144 amino acids. To investigate the mechanisms involved in processing of the protein encoded by HEV1, three domain-specific antisera were raised against fusion proteins harboring the amino-terminal domain (N domain), carboxyl-terminal domain (C domain), and both domains (NC domain). Translocation expts. using an in vitro

translation system show that the first 17-amino acid sequence encoded by the cDNA functions as a signal peptide. Immunoblot anal. of proteins extracted from lutoid bodies demonstrates that a 5-kDa protein comigrated with purified mature hevein and cross-reacted with N domain- and NC domain-specific **antibodies**. A 14-kDa protein was recognized by C domain- and NC domain-specific **antibodies**. A 20-kDa protein was cross-reactive with all three **antibodies**. Microsequencing data further suggest that the 5-kDa (amino-terminal domain and 14-kDa (carboxyl-terminal domain) proteins are post-translational cleavage products of the 20-kDa polypeptide (both domains) which corresponds to the **proprotein** encoded by HEV1. In addition, it was found that the amino-terminal domain could provide chitin-binding properties to a fusion protein bearing it either amino terminally or carboxyl terminally.

L10 ANSWER 24 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 10
AN 1989:493738 CAPLUS
DN 111:93738
TI Membrane protein sorting: biosynthesis, transport and processing of yeast vacuolar alkaline phosphatase
AU Klionsky, Daniel J.; Emr, Scott D.
CS California Inst. Technol., Pasadena, CA, 91125, USA
SO EMBO Journal (1989), 8(8), 2241-50
CODEN: EMJODG; ISSN: 0261-4189
DT Journal
LA English
AB The Saccharomyces cerevisiae PHO8 gene product, repressible alkaline phosphatase (ALP), is a glycoprotein enzyme that is localized to the yeast vacuole (lysosome). Using **antibodies** raised against synthetic peptides corresponding to 2 distinct hydrophilic sequences in ALP, the biosynthesis, sorting, and processing of this protein were examined ALP is synthesized as an inactive precursor containing a C-terminal **propeptide** that is cleaved from the protein in a PEP4-dependent manner. The precursor and mature proteins are anchored in the membrane by an N-terminal hydrophobic domain that also appears to function as an uncleaved internal **signal sequence**. ALP has the topol. of a type-II integral membrane protein containing a short basic N-terminal cytoplasmic tail that is accessible to exogenous protease when associated both with the endoplasmic reticulum and the vacuole. Similar to the soluble vacuolar hydrolases carboxypeptidase Y (CPY) and proteinase A (PrA), ALP transits through the early stages of the secretory pathway prior to vacuolar delivery. Two observations indicate, however, that ALP is localized to the vacuole by a mechanism which is in part different from that used by CPY and PrA: maturation of proALP, which is indicative of vacuolar delivery, is less sensitive than CPY and PrA to the defects exhibited by certain of the vacuolar protein sorting mutants; and maturation of proALP proceeds normally in the presence of a potent vacuolar ATPase inhibitor, bafilomycin A1, which is known to block vacuole acidification and leads to the mis-sorting and secretion of precursor forms of CPY and PrA. These results indicate that ALP will be a useful model protein for studies of membrane protein sorting in yeast.

L10 ANSWER 25 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 11
AN 1989:4378 CAPLUS
DN 110:4378
TI Synthesis, processing, and transport of Pseudomonas aeruginosa elastase
AU Kessler, Efrat; Safrin, Mary
CS Sackler Fac. Med., Tel Aviv Univ., Tel Hashomer, 52621, Israel
SO Journal of Bacteriology (1988), 170(11), 5241-7
CODEN: JOBAAY; ISSN: 0021-9193
DT Journal
LA English
AB Three cell-associated elastase precursors with approx. mol. wts. of 60,000 (P), 56,000 (Pro I), and 36,000 (Pro II) were identified in Pseudomonas aeruginosa cells by pulse-labeling with [35S]methionine and immunopptn.

In the absence of inhibitors, cells of a wild-type strain as well as those of the secretion-defective mutant PAKS 18 accumulated Pro II as the only elastase-related radioactive protein. EDTA but not EGTA inhibited the formation of Pro II, and this inhibition was accompanied by the accumulation of Pro I. P accumulated in cells labeled in the presence of ethanol with or without EDTA), dinitrophenol plus EDTA, or CCCP plus EDTA. Pro I and Pro II were localized to the periplasm, and as evident from pulse-chase expts., Pro I was converted to the mature extracellular enzyme with Pro II as an intermediate of the reaction. P was located to the membrane fraction. Pro I but not Pro II was immunopptd. by **antibodies** specific to a protein of about 20,000 mol. weight (P20), which, as showed before (Kessler, E., and Safrin, M., 1988), forms a complex with an inactive periplasmic elastase precursor of about 36,000 mol. weight Apparently, the elastase is made by the cells as a preproenzyme (P), containing a **signal sequence** of about 4000 mol. weight and a "pro" sequence of about 20,000 mol. weight Processing and export of the preproenzyme involve the formation of two periplasmic proenzyme proelastase II accumulates temporarily in the periplasm, most likely as a complex with the 20-kDa **propeptide** released from proelastase I upon conversion to proelastase II. The final step in elastase secretion seems to require both the proteolytic removal of a small peptide from proelastase II and dissociation of the latter from P20.

L10 ANSWER 26 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 12
AN 1989:434395 CAPLUS
DN 111:34395
TI Structure of the precursor to an enzyme mediating carboxy-terminal amidation in peptide biosynthesis
AU Eipper, Betty A.; Park, Larry P.; Dickerson, Ian M.; Keutmann, Henry T.; Thiele, Elizabeth A.; Rodriguez, Henry; Schofield, Peter R.; Mains, Richard E.
CS Sch. Med., Johns Hopkins Univ., Baltimore, MD, 21205, USA
SO Molecular Endocrinology (1987), 1(11), 777-90
CODEN: MOENEN; ISSN: 0888-8809
DT Journal
LA English
AB Many bioactive peptides terminate with an amino acid α-amide at their COOH terminus. The enzyme responsible for this essential posttranslational modification is known as peptidyl-glycine α-amidating monooxygenase or PAM. Some cDNAs encoding the enzyme were identified by using **antibodies** to screen a bovine intermediate pituitary λgt11 expression library. **Antibodies** to a β-galactosidase/PAM fusion protein removed PAM activity from bovine pituitary homogenates. The 108,207 dalton protein predicted by the complete cDNA is approx. twice the size of purified PAM. An NH2-terminal **signal sequence** and short **propeptide** precede the NH2 terminus of purified PAM. The sequences of several PAM cyanogen bromide peptides were localized in the NH2-terminal half of the predicted protein. The cDNA encodes an addnl. 430 amino acid intragranular domain followed by a putative membrane spanning domain and a hydrophilic cytoplasmic domain. The forms of PAM purified from bovine neurointermediate pituitary may be generated by endoproteolytic cleavage at a subset of the 10 pairs of basic amino acids in the precursor. High levels of PAM mRNA were found in bovine pituitary and cerebral cortex. In corticotropic tumor cells, levels of PAM mRNA and pro-ACTH/endorphin mRNA were regulated in parallel by glucocorticoids and CRF.

L10 ANSWER 27 OF 27 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 13
AN 1985:539255 CAPLUS
DN 103:139255
TI Sequence of the precursor to rat bone γ-carboxyglutamic acid protein that accumulates in warfarin-treated osteosarcoma cells
AU Pan, Lydia C.; Williamson, Matthew K.; Price, Paul A.

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CS   Dep. Biol., Univ. California, La Jolla, CA, 92093, USA
SO   Journal of Biological Chemistry (1985), 260(25), 13398-401
     CODEN: JBCHA3; ISSN: 0021-9258
DT   Journal
LA   English
AB   A biosynthetic precursor to rat bone γ-carboxyglutamic acid-containing
     protein (BGP) was isolated from warfarin-treated ROS 17/2 osteosarcoma
     cells by antibody affinity chromatog. followed by reverse-phase
     HPLC.  Thirty-two residues of the N-terminal sequence of BGP precursor
     were determined by gas-phase protein sequence anal.  Comparison of this
     sequence with the known structure of rat BGP established that the
     intracellular precursor is a 76-residue mol. of mol. weight 9120 that differs
     from 6000-dalton bone BGP in having an N-terminal extension of 26
     residues.  This precursor appears to be generated from the primary
     translation product by cleavage of a hydrophobic signal peptide and is the
     probable substrate for γ-carboxylation by virtue of its accumulation
     in the presence of warfarin.  The putative targeting region for
     γ-carboxylation previously identified in the  leader
     sequences of vitamin K-dependent proteins is found in the
     propeptide portion of the precursor.  Since the immunoreactive
     component secreted by warfarin-treated cells is identical in sequence to
     the 6000-dalton BGP from bone, propeptide cleavage from the
     precursor is independent of γ-carboxylation and precedes secretion
     of BGP from the cell.


=> d his

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L3         29266 S ((SIGNAL OR LEADER) (W) SEQUENCE)
L4             0 S L1 AND L2 AND L3
L5          9391 S PROPEPTIDE OR PROPROTEIN
L6             0 S L1 AND L3 AND L5
L7             2 S L2 AND L5
L8           411 S L3 AND L5
L9            44 S (ANTIBODY OR (FAB (W) FRAGMENT)) AND L8
L10           27 DUPLICATE REMOVE L9 (17 DUPLICATES REMOVED)

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=> s ((Fab (w) fragment) and L8)
L11          0 ((FAB (W) FRAGMENT) AND L8)
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CS   Dep. Biol., Univ. California, La Jolla, CA, 92093, USA
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     CODEN: JBCHA3; ISSN: 0021-9258
DT   Journal
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AB   A biosynthetic precursor to rat bone γ-carboxyglutamic acid-containing
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L11          0 ((FAB (W) FRAGMENT) AND L8)
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#4	Search **Fd and Fab** Limits: **Publication Date to 2002/10/3**	11:30:49	160
#3	Search **Fd and Fab and propeptide** Limits: **Publication Date to 2002/10/3**	11:30:41	0
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